`

Assessment of coronary artery disease using multiparametric cardiac magnetic resonance imaging

A dissertation submitted in partial fulfillment of MD Radiodiagnosis (Branch VIII) examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in April 2016

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A study to assess the presence and extent of myocardial ischemia and infarction using multiparametric cardiac MRI scan and correlation with echocardiography and conventional coronary angiography, in patients with suspected or diagnosed coronary artery disease, in a tertiary care centre in South India.

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DECLARATION

I declare that the dissertation entitled "Assessment of coronary artery disease using multiparametric cardiac magnetic resonance imaging" is my original work done in partial fulfillment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in April 2016

Dr. Subin Kuruvilla Thomas
Post graduate student (MD Radiodiagnosis)
Department of Radiodiagnosis
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CERTIFICATE

This is to certify that the dissertation entitled “Assessment of coronary artery disease using multiparametric cardiac magnetic resonance imaging” is the bonafide original work of Dr. Subin Kuruvilla Thomas submitted in partial fulfillment of the requirement for MD Radiodiagnosis (Branch VIII) Degree Examination of the Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in April 2016

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Professor

Department of Radiodiagnosis

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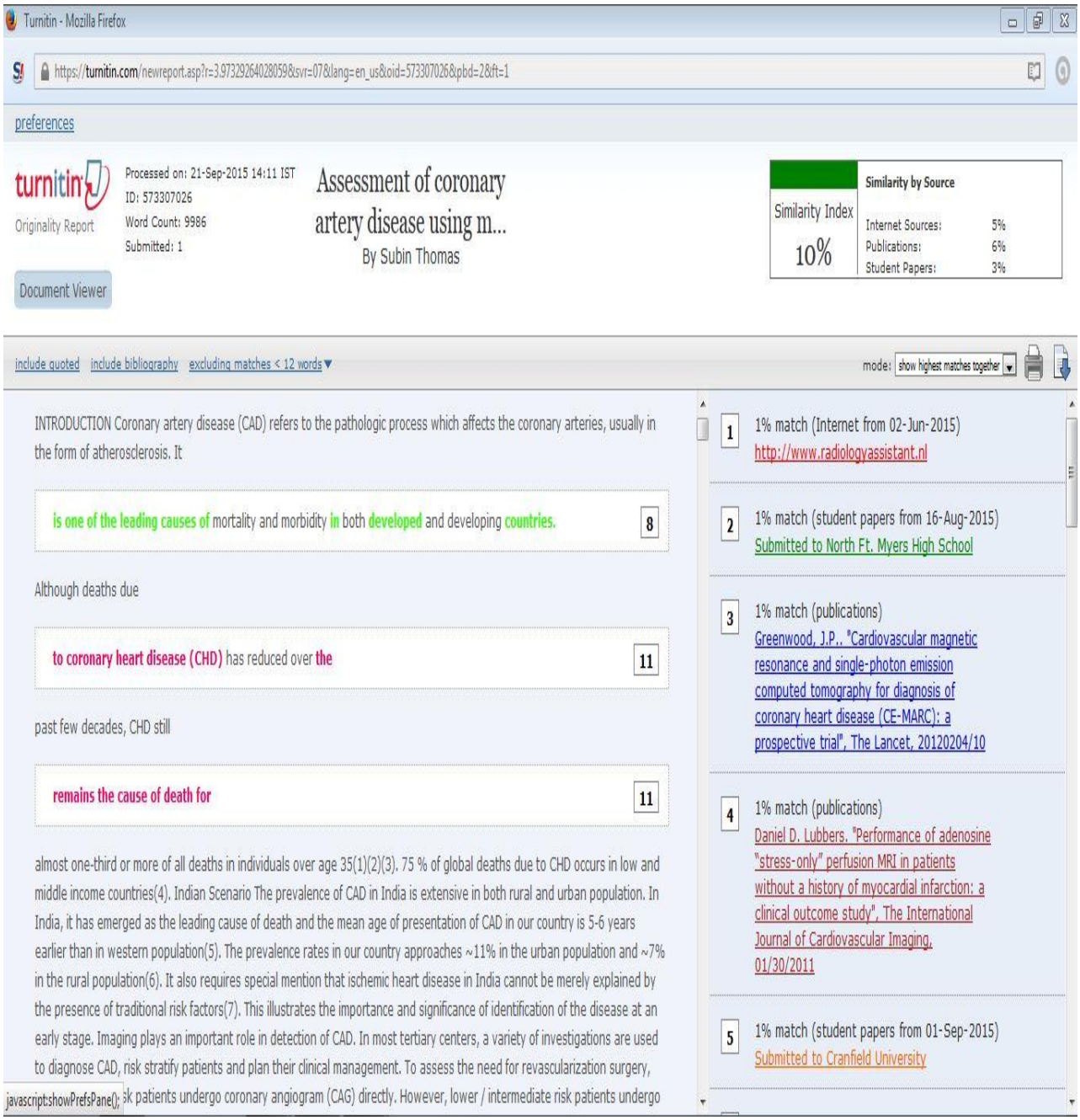

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INTRODUCTION

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July 25, 2014

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Sub: **Fluid Research grant project:**
A study to assess the presence and extent of myocardial ischemia and infarction using multiparametric cardiac MRI scan and correlation with ECG,echocardiography and conventional coronary angiography, in patients with suspected or diagnosed coronary artery disease, in a tertiary care center in South India.
Dr. Subin Kuruvilla Thomas, PG Registrar, Radiology, Dr. Elizabeth Joseph, Radiology, Dr. Viji Samuel, Cardiology, Dr. Oommen George, Cardiology, Dr. Paul George, Cardiology.

Ref: IRB Min No: 8724 [OBSERVE] dated 06.03.2014

Dear Dr. Subin Kuruvilla Thomas,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD.,MNAMS.,DNB(Endo),FRACP(Endo),FRCP(Edin),FRCP(Glasg)
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Dear Dr. Subin Kuruvilla Thomas,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "A study to assess the presence and extent of myocardial ischemia and infarction using multiparametric cardiac MRI scan and correlation with ECG,echocardiography and conventional coronary angiography, in patients with suspected or diagnosed coronary artery disease, in a tertiary care center in South India." on March 06th 2014.

The Committees reviewed the following documents:

1. IRB Application format
2. Curriculum Vitae' of Drs. Subin Kuruvilla Thomas, Elizabeth Joseph, Viji Samuel, Oommen George, Paul George
3. Informed Consent form (English, Tamil, Telugu & Bengali)
4. Information Sheet (English, Tamil, Telugu & Bengali)
5. No of documents 1-4

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
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The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on March 6th 2014 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Other Affiliations
Dr. T. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician
Dr. J. Visalakshi	MPH, PhD	Lecturer, Dept. of Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Ranjith K Moorthy	MBBS M Ch	Professor, Neurological Sciences, CMC, Vellore	Internal, Clinician
Dr. Chandra Singh	MS, MCH, DMB	Professor, Urology, CMC, Vellore	Internal, Clinician
Dr. Paul Ravindran	PhD, Dip RP, FCCPM	Professor, Radiotherapy, CMC, Vellore	Internal, Clinician
Dr. Bobby John	MBBS, MD, DM, Ph D, MAMS	Professor, Cardiology, CMC, Vellore	Internal, Clinician
Dr. Anup Ramachandran	Ph. D	The Wellcome Trust Research Laboratory Gastrointestinal Sciences, CMC, Vellore	Internal, Basic Medical Scientist
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician
Dr. Niranjan Thomas	DCH, MD, DNB (Paediatrics)	Professor, Neonatology, CMC, Vellore	Internal, Clinician
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Dr. Shirley David	M.Sc, PhD	Professor, Head of Fundamentals Nursing Department, CMC, Vellore	Internal, Nurse
Mrs. Pattabiraman	B. Sc, DSSA	Social Worker, Vellore	External, Lay person
Mr. C. Sampath	B. Sc, BL	Legal Expert, Vellore	External, Legal Expert
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Dr. Vathsala Sadan	M.Sc, PhD	Professor, Community Health Nursing, CMC, Vellore	Internal, Nurse
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Dr. Nihal Thomas	MD, MNAMS, DNB(Endo), FRACP(Endo) FRCP(Edin) FRCP (Glasg)	Professor & Head, Endocrinology. Additional Vice Principal (Research), Deputy Chairperson, IRB, Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician

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Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

Fluid Grant Allocation:

A sum of 95,200/- INR (Rupees Ninety Five Thousand Two Hundred only) will be granted for 19 months.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

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And to the Lord Almighty for all his blessings, throughout my life.

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TABLE OF CONTENTS

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INTRODUCTION

Coronary artery disease (CAD) refers to the pathologic process which affects the coronary arteries, usually in the form of atherosclerosis. It is one of the leading causes of mortality and morbidity in both developed and developing countries. Although deaths due to coronary heart disease (CHD) has reduced over the past few decades, CHD still remains the cause of death for almost one-third or more of all deaths in individuals over age 35(1)(2)(3). 75 % of global deaths due to CHD occurs in low and middle income countries(4).

Indian Scenario

The prevalence of CAD in India is extensive in both rural and urban population. In India, it has emerged as the leading cause of death and the mean age of presentation of CAD in our country is 5-6 years earlier than in western population(5). The prevalence rates in our country approaches ~11% in the urban population and ~7% in the rural population(6). It also requires special mention that ischemic heart disease in India cannot be merely explained by the presence of traditional risk factors(7). This illustrates the importance and significance of identification of the disease at an early stage. Imaging plays an important role in detection of CAD.

In most tertiary centers, a variety of investigations are used to diagnose CAD, risk stratify patients and plan their clinical management. To assess the need for revascularization surgery, majority of high risk patients undergo coronary angiogram (CAG) directly. However, lower / intermediate risk patients undergo non-invasive

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tests like exercise tolerance testing (ETT), stress echocardiography, SPECT scan or stress cardiac MRI, in order to identify those most likely to require coronary revascularization.

Gold standard:

Invasive catheter coronary angiography is currently the gold standard in detection of coronary artery disease. Results are classified as follows, lesions < 50% being minor; 50-69% being intermediate and >70% indicating significant occlusion. Those having significant occlusion of >70% are considered for revascularization procedure. Lesions are measured by visual estimates or by QCA (quantitative coronary analysis) which is incorporated in the PHILIPS lab systems. For suspicious intermediate lesions (50-69%), revascularization is recommended only if one of the other non-invasive tests positive for reversible ischemia. The rest are on medical treatment and on routine follow up.

However, catheter angiography is limited by its invasive nature, procedural risks, inability to assess the microcirculation, lack of functional data, and cost. The evaluation of patients presenting with chest pain including those with known or suspected CAD often includes non-invasive testing.

Available Non-Invasive Tests

A variety of non-invasive tests are available and the performance of each modality is defined by comparing the test results with that of invasive catheter angiography (gold

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standard). The following tests are available for the non-invasive testing of coronary artery disease:

- Exercise ECG, generally using a treadmill and standardized protocols.
- Stress echocardiography using either pharmacological agents (dobutamine or dipyridamole) or exercise
- Radionuclide myocardial perfusion imaging using either exercise or pharmacologic stress and imaging with either SPECT or positron emission tomography (PET)
- Coronary CT angiography (CCTA)
- Hybrid imaging using SPECT/CT, PET/CT, or PET/MR.
- Stress cardiac MRI (using adenosine or dobutamine)

Exercise ECG testing

Exercise ECG testing, most often involving treadmill exercise, is a commonly used non-invasive test because it is widely available, accessible, simple, inexpensive and well-validated.

The advantage includes not only the fact that it is more physiological and mimics the conditions under which the patient's usual symptoms may be replicated but also that it documents the workload that induces symptoms of ischemia. The exercise capacity

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and hemodynamic responses assessed during the study are predictors of prognosis which are independent of ischemia. However, it cannot be interpreted for the development of ischemia in the presence of certain baseline abnormalities, including: left bundle branch block, paced ventricular rhythm, LV hypertrophy with abnormalities in repolarization, ST-segment depression of ≥1 mm and ventricular pre-excitation(8).

Stress echocardiography

It can be performed with a variety of stress modalities (exercise or more commonly dobutamine) and does not involve radiation exposure to the patient. It provides information regarding the global left ventricular function, ischemic territory and extent of ischemia that is not acquired from exercise ECG testing alone. However, there are limitations. One limitation is the potential for rapid resolution of ischemia prior to image acquisition post-exercise. Additionally, a hypertensive response to exercise can be associated with a greater chance of a false positive exercise stress ECHO. Suboptimal acoustic window is also a problem.

Stress radionuclide myocardial perfusion imaging (using SPECT)

It provides information regarding the extent, severity, and location of the ischemic territory that is generally not acquired from exercise ECG testing alone. Detection of myocardial perfusion defects also increases the specificity and sensitivity for the diagnosis of CAD over clinical characteristics and exercise test results. Stress rMPI

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also provides measurements of left ventricular volumes and global and regional function. This test can be used in patients who are unable to exercise to an adequate level (by substituting a vasodilator or dobutamine as the stress agent) as well as those with resting ECG abnormalities which preclude exercise ECG testing alone.

Stress cardiac magnetic resonance imaging

This can be performed using either a vasodilator stress agent such as adenosine or dobutamine. It has the ability to provide information on cardiac structure, global and regional left and right ventricular function, infarct size, location, transmurality and myocardial ischemia through pharmacologic stress. CMR uses no ionizing radiation. The advantages of CMR include high spatial resolution, lack of radiation exposure, and its multiparametric nature—that is, its ability to assess multiple aspects of the pathology in a single study (eg, ejection function, myocardial perfusion, viability and even coronary artery anatomy)

Comparison with SPECT:

A recent prospective trial known as the CE-MARC trial was done to assess the diagnostic accuracy of a multiparametric CMR with coronary angiography as a reference standard and also to compare Cardiac MR with SPECT scan. It was done in patients suspected to have CAD. In the 752 recruited patients, 39% had significant CHD as detected by x-ray angiography. Multiparametric CMR showed a sensitivity of 86·5%, specificity of 83·4%, positive predictive value of 77·2% and negative

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predictive value of 90·5%. The sensitivity of SPECT was only 66·5% while specificity was 82·6%, positive predictive value was 71·4% and negative predictive value was 79·1%. The sensitivity and negative predictive value of Cardiac MR and SPECT showed significant difference (with p value <0·0001) but specificity and positive predictive value did not differ much (p=0·916 and p=0·061, respectively).

This landmark trial has established Cardiac MRI's high diagnostic accuracy in identifying CAD and cardiac MR's superiority over SPECT(9).

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AIMS AND OBJECTIVES

Aim of the study

To assess the burden of coronary artery disease in patients with suspected or diagnosed CAD who are referred for adenosine stress cardiac MRI

Primary objectives:

1. To detect myocardial ischemia by inducing vasodilator mediated stress on the heart by injecting adenosine
2. To compare stress and rest perfusion deficits in order to distinguish true ischemia from infarcts / artifacts
3. To detect established myocardial infarction as evidenced by late gadolinium enhancement
4. To assess the correlation between adenosine stress MRI and coronary angiogram in patients with positive stress test

Secondary objectives:

1. To compare regions / segments of myocardial ischemia and infarction, identified by adenosine stress cardiac MRI with coronary angiogram in the same patient
2. To estimate the left ventricular ejection fraction (LVEF) and identify segments of regional wall motion abnormality (RWMA) using cardiac MRI.

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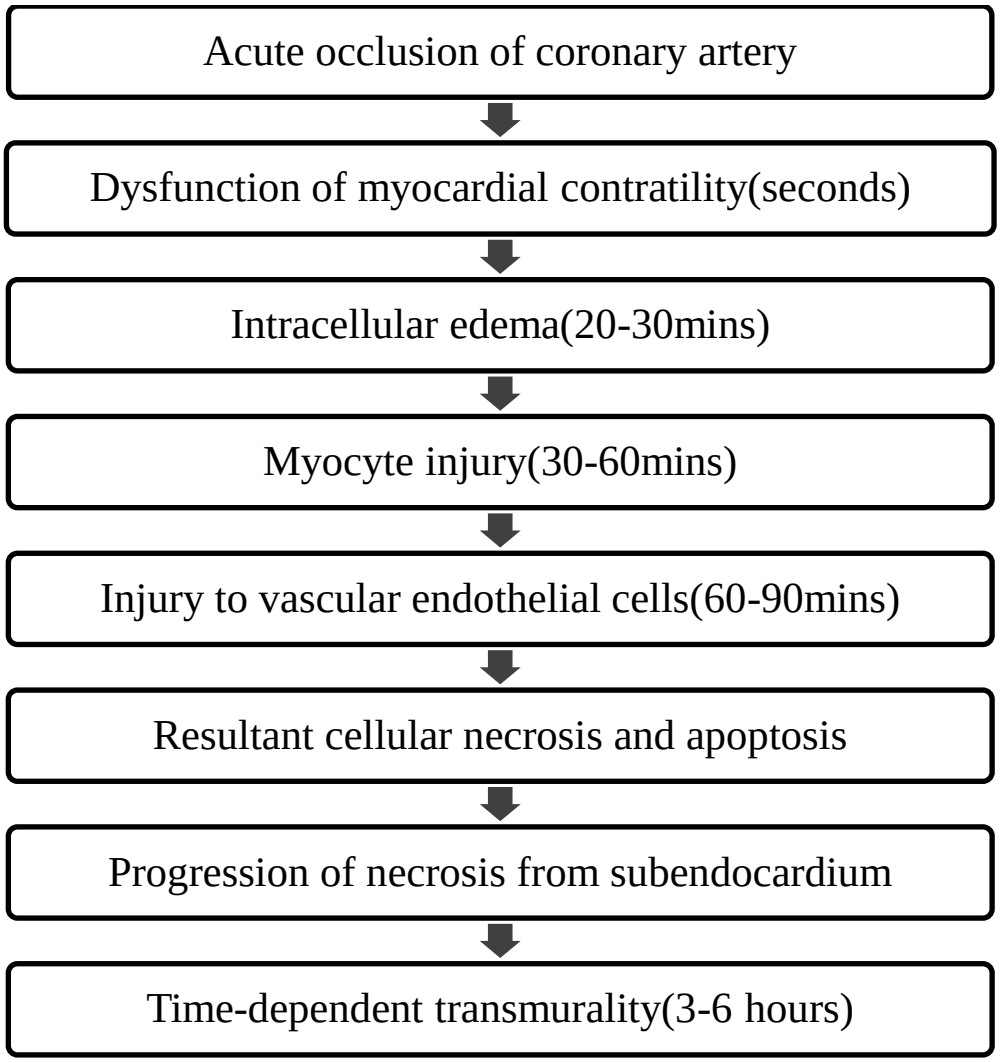
REVIEW OF LITERATURE:

Improved therapeutic drugs and prevention campaigns have resulted in a decline in the mortality rate of ischemic heart disease (IHD) in the recent years. However, IHD still remains the most leading cause of death in adults and it is likely to continue in increasing prevalence(10). This has urged the need for a good diagnostic and prognostic tool. MRI has emerged as an important tool in the clinical and pre-clinical detection of IHD as well as in prognostication(11).

Pathophysiology of myocardial ischemia and infarction



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The "*myocardium at risk*" or "jeopardized myocardium" refers to the area of myocardium in the perfusion territory of the affected artery distal to the critical lesion(12)(13).

Current therapeutic measures involve immediate restoration of the affected epicardial blood flow which aims to salvage the viable myocardium at risk. However, the reperfusion may also cause "*myocardial reperfusion injury*" wherein the cell damage may continue in the first few hours. This occurs mainly due to the presence of microvascular obstruction wherein, despite successful establishment of epicardial flow, there is complete absence of tissue perfusion.

"S*tunned myocardium*" is prolonged dysfunction of contractility occurring after a short ischemic attack and this can be salvaged after reperfusion. This may take days or weeks to normalize, though it can be also reversed using inotropic agents. It was originally used to describe the condition demonstrated in the laboratory in which complete coronary artery occlusion lasting only 5 to 15 minutes (reversible stage) produced regional wall motion abnormality that persisted for hours or days following reperfusion(14).

"*Hibernating myocardium*" is viable myocardium in a state of persistent myocardial dysfunction, secondary to a chronically reduced blood flow. It can be partially or completely restored back to normal either by increasing the blood flow or by reducing oxygen demand. This phenomenon was recognized from a clinical observation made more than 30 years ago by clinicians when they noticed that chronic myocardial dysfunction present before a bypass surgery did improve after revascularization. (15)

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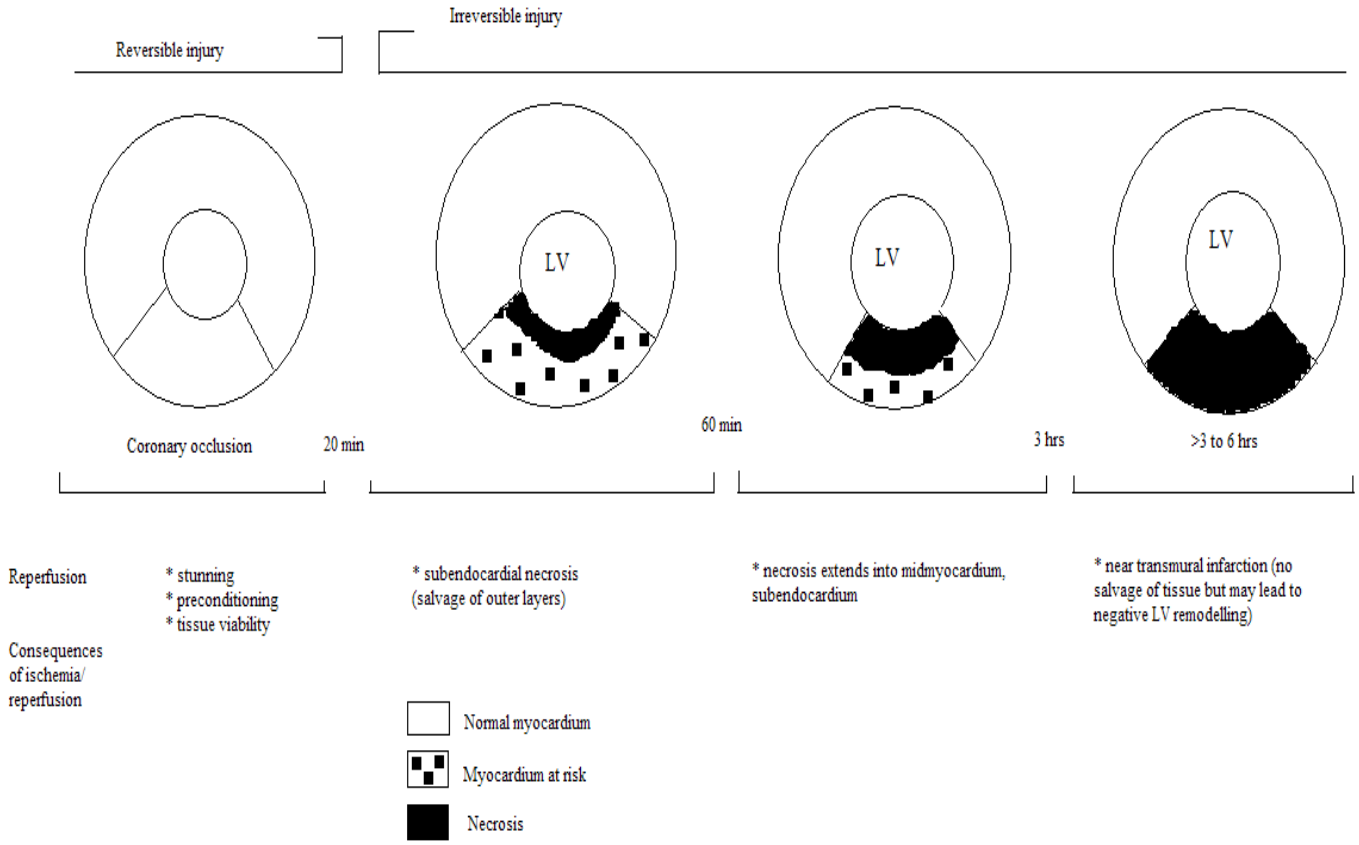

Illustration of effect of ischemia and reperfusion on myocardial viability and necrosis

Rationale for stress testing

Management of CAD in a patient with decreased left ventricular function and poor quality of life and with increased risk for sudden cardiac death involves a multi-level strategy. The most important of all is primary prevention which involves increasing awareness about CAD and educating people about its risk factors and its various modes of presentation. This aims at reducing the preventable risk factors such as smoking, diabetes mellitus, obesity, dyslipidemia, hypertension, physical inactivity and high stress. Secondary prevention involves the management of both preventable and non-preventable risk factors of CAD. This includes methods like cessation of

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smoking, drug therapy, exercise and diet control for hypertension, diabetes and dyslipidemia. Tertiary prevention is the management of the disease manifestation itself. This includes surgery and angioplasty to reduce the morbidity of the already existing disease. Patients undergo investigations like ECG, ECHO and coronary angiography as a part of work up for diagnosis of the disease.

Relatively few patients suffering from CAD can be resuscitated from sudden death. Therefore, most of the effort goes in detecting coronary artery disease at an earlier stage and in preventing permanent myocardial damage. Stress testing of the heart is one of the most powerful tools in detecting CAD at an early stage.

Multiple methods are available to detect CAD. These include both invasive and non-invasive tests. The gold standard is invasive coronary angiogram. Most non-invasive tests use technologies which do not directly image coronary arteries except for CT/MR coronary angiogram. The common non-invasive tests include stress ECG (Treadmill test), stress echocardiography, stress SPECT/PET (exercise or pharmacological) and pharmacological stress MRI.

A patient with coronary artery disease can have symptoms of chest discomfort in two major presentations. One is an acute coronary syndrome (ACS) wherein a thrombus forms over an unstable coronary plaque and causes intermittent or complete occlusion of the affected coronary artery. This, in the most extreme cases, may present as acute ST elevation myocardial infarction. The second presentation is that in a patient with unstable angina wherein no permanent myocardial damage may have occurred but

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further testing using coronary angiogram or stress testing may be required to explain the symptoms and also to determine the need for an intervention.

Except in cases of acute myocardial infarction or the most severe rest perfusion defects associated with a hibernating myocardium, the rest perfusion of the heart remains generally normal. Even in a setting of severe coronary artery stenosis, normal blood supply may be maintained to the myocardium through methods of auto regulation. Therefore, at rest a patient can be normal without any chest pain. Rest perfusion images also look normal and uniform in such cases.

Stress testing challenges the heart's ability to regulate its myocardial blood supply and uncovers coronary artery stenosis. This may be done either by exercise or by use of pharmacological agents. Exercise and vasodilator medicines (such as adenosine) increase the blood flow through the normal coronaries. However, the downstream blood flow cannot increase much if there is a significant stenosis in the proximal artery. Thus, exercise can induce chest pain or ST segment abnormalities while in a stress perfusion study, a relative perfusion defect may be seen using SPECT or cardiac MRI study.

Alternatively, imaging can also be used to detect a worsening or new wall motion abnormality. This method is used in stress (using exercise or dobutamine) echocardiography and dobutamine stress MRI.

Stress imaging studies are generally indicated when a patient has an uninterpretable ECG (due to baseline ST segment abnormalities) or equivocal stress ECG.

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Pharmacological stress testing is done when patients cannot exercise. In exercise stress testing, the patient's heart rate has to peak upto 85% of the maximal predicted for his/her age. This might be difficult to achieve in patients with problems such as arthritis.

The other alternative is to directly image the coronary vessels. However, direct imaging by invasive coronary angiogram is reserved for people with high index of suspicion for coronary artery stenosis. Moreover, in cases of intermediate stenosis, it is necessary to determine using stress testing as to whether it is physiologically significant or not. Even with high grade stenosis of >70%, the fractional flow reserve may be normal indicating that the stenosis is not physiologically significant. Thus, there is an increasing need to determine the physiological significance of coronary stenosis (16).

Cardiac risk factors play an important role in guiding preventive strategies and treatment methods. However, their short term predictive value for coronary artery disease is relatively weak. This makes them unsuitable for planning treatment strategies.

In summary, stress testing is important for detecting coronary artery disease in low and intermediate risk patients and also to assess the physiological significant of coronary stenosis.

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Rationale for viability imaging

The term infarction or loss of viability refers to a state where the myocyte death has occurred. All ischemic events, preceding cell death, are potentially reversible. Presence or absence of cell death can be proved by light or electron microscopy, or with the use of histologic stains. However, in-vivo testing for myocardial viability by microscopy or histologic staining is not obviously practical. Less precise definitions of viability include the use of parameters such as wall motion abnormality, presence of Q waves, loss of myocyte integrity and changes in tissue composition(17). The knowledge of viable myocardium is important as it reflects the direction of patient management in a setting of coronary artery disease.

A meta-analysis of 3088 patients from 24 viability studies done using thallium perfusion imaging, F-18 fluorodeoxyglucose metabolic imaging or dobutamine echocardiography, reported that revascularization, as compared with medical therapy, achieved 79.6 percent reduction in mortality. The average annual mortality in such patient after revascularization and medical therapy were 3.2% and 16%, respectively. Patients with low viability fared poorly irrespective of therapy (annual mortality 7.7 and 6.2 percent respectively)(18)

The main role for the non-invasive assessment of viability and hibernating myocardium is in the more severely and chronically disabled group of patients who has poor outcome if intervention is not done but with high risk of revascularization(19). Hibernating myocardium is relevant in patients with heart

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failure without limiting angina and in such patients, revascularization is aimed at improving the left ventricular function rather than to treat ischemia(20).

Non-invasive viability testing may be done using various indirect parameters for assessment of myocardial viability:

- Response to inotropic stimulation to detect wall motion abnormality(dobutamine)
- Recovery of contractile function after revascularization
- Presence of normal glucose metabolism (FDG-PET)
- Presence of active cellular transport (SPECT)
- Absence of scarred (fibrosed) myocardium (Contrast enhanced MRI)

SPECT and MRI are well established modalities for viability assessment.

SPECT IMAGING

It uses radiopharmaceuticals such as Thallium-201 or Tc-99m-sestamibi. The uptake of thallium-201 by the myocardium is a sarcolemmal membrane Na/K ATPase-dependent active process requiring active cell membrane integrity. This is therefore, indicative of viability of the myocardium. First pass perfusion of Thallium-201 into the myocytes is a reflection of regional perfusion (required for delivery of tracer to the myocyte) making it possible to detect ischemic areas as well. The presence of an

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intact sarcolemmal and mitochondrial membrane is required for the uptake and retention of Technetium-99m (Tc-99m) sestamibi. This makes it a good tracer for assessment of regional cellular viability.

CARDIAC MRI FOR VIABILITY

Magnetic resonance imaging has an established role in cardiovascular imaging. It provides important information on anatomy, function as well as blood flow. It provides two ways to assess patients with coronary disease. One is to assess the morphology of the myocardium (which includes measurement of myocardial thickness) myocardial function (ejection fraction) at rest and contratile reserve using pharmacological stress agents. The second method is to image the infarcted myocardium and assess the microcirculation using a contrast agent.

MRI can provide high resolution and high contrast images which makes it a great technique for measuring ventricular volumes, myocardial mass, ejection fraction and regional wall motion (21)(22). Upto 1-2 mm of spatial resolution and temporal acquisition of 20-50ms can be achieved. It is able to distinguish transmural variations in viability, accurately defining the extent of necrosis. There is therefore no suggestion that the technique will either overestimate or underestimate the extent of myocardial infarction. This is one of its strongest points as the spatial resolution in scintigraphy or PET imaging is relatively poor.

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Before the arrival of gadolinium contrast, there were two main principles for myocardial viability testing: function and metabolism. The former principle is used in dobutamine stress testing wherein the improvement in function from rest to 10-20ug/kg/min of dobutamine serves as a marker for viability(23). This may be done either using echocardiography or magnetic resonance imaging. The second principle is used in PET imaging which demonstrates uptake of radioactive labeled glucose(24).

Introduction of gadolinium contrast has established a new principle: late gadolinium enhancement imaging (LGE). Gadolinium DTPA is the commonly used tracer.

Gadolinium Contrast Agents

Gadolinium (Gd) is an element which is toxic in its unbound state. Contrast agents are made of a large molecule which keeps the gadolinium molecule bound to itself. These carrier molecules are large in size and do not enter the intracellular space. Thus, they are extracellular contrast agents. The ideal agent has to be stable (does not release the bound Gd), should be able to increase the signal intensity to the maximum and also should be water soluble so that it can be easily administered.

These contrast agents are commonly excreted by the kidneys, with a half-life of 2 hours. They are completely cleared from the blood after 24 hours. Gadolinium was considered as a safe drug for many years but now we know of an entity known as ‘nephrogenic systemic fibrosis. It is a severely debilitating disease which resembles scleroderma and it most commonly seen in patients with decreased renal function.

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However, after laying down strict guidelines for the use of these contrast agents in those with low renal function, the number of cases have drastically reduced(25).

MRI imaging - late gadolinium enhancement

Gadolinium contrast agent is restricted to extravascular and interstitial spaces and thus accumulates in the infarcted tissue due to the loss of membrane integrity in the form of sarcolemmal break down. The accumulation is further encouraged by the delayed wash out of contrast. The delayed washout of the contrast is due to suboptimal or poor venous drainage in these regions. Thus, increased signal intensity of gadolinium-DTPA in delayed imaging is specific to myocardium that is infarcted.

Gadolinium is a paramagnetic agent which reduces the T1 time. T1 weighted sequences like FLASH can be used. However, inversion recovery sequence wherein the normal myocardium is nulled is the best method. The technique is to inject 0.1-0.2 mmol/kg bolus of Gd-based contrast, and after 10-20 minutes, T1 scout image is obtained. From the T1 scout image, the adequate inversion time (TI) to null the normal myocardium is chosen. It is very important is choose the correct inversion time for best diagnostic quality. Optimal inversion time can vary from person to person and in accordance with factors such as cardiac output and dosage of contrast. The optimal TI is that which results in complete suppression of signal from the normal myocardium along with a bright signal from the myocardial cavity and an even brighter signal in the infarcted tissue. Selecting the correct inversion time can

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accurately differentiate between endomyocardial, midmyocardial and subendocardial late gadolinium enhancement and also to visualize intraluminal thrombus. The introduction of phase sensitive inversion recovery sequence (PSIR) has allowed the acquisition of delayed images without having to pick a precise inversion time(26).

Typically, the hyperenhancement is subendocardial or transmural in a coronary artery distribution. This hyperenhancement correlates on histopathology to fibrosis (scarring) and it will not recover function post revascularization(27). This lead to the concept of "bright is dead". This is in reference to the high signal intensity of the infarcted tissues. With this delayed imaging technique, infarcts upto 2 gram on average can be detected (28).

A study by Kim et al described the relationship of delayed enhancement in cardiac MRI to irreversible injury, infarct age (both in acute or chronic) and the contractile function of the myocardium in mongrel dogs. Contrast enhancement of myocardium that was injured in acute infarction after induced severe but reversible ischemia was compared with contrast enhancement of myocardium in chronic infarction state. The results proved that both acute and chronic myocardial infarcts enhance on the delayed contrast images. The spatial extent of hyperenhancement was in concordance with the spatial extent of myocyte necrosis seen on histology. Stunned myocardium did not enhance. Thus, this study established that infarcted or non-viable myocardium shows delayed enhancement while viable tissue does not show enhancement. The study concluded that contrast enhanced MRI can distinguish between reversible and

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irreversible ischemic injury and that the identification of reversible versus irreversible myocardium is likely to be independent of the wall motion and infarct age(27).

Kim and colleagues studied patients with left ventricular dysfunction scheduled for surgical or percutaneous revascularization and found a progressive decrease in the likelihood of improvement post-revascularization with increase in transmural extent of hyperenhancement. The myocardial contractility increased in 78% of segments in the absence of delayed enhancement. But the contractility increased only in 1 of 58 segments with delayed hyperenhancement in >75% of wall thickness(29). More studies have also confirmed these findings(30).

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STRESS CARDIAC MRI

Techniques

Cardiac MRI uses the same principles as other MRI techniques but uses ECG gating in addition. Among the many techniques employed on MRI systems, below mentioned three are the mainstays of clinical CMR:

- Spin echo imaging: This technique depicts the heart tissue as bright and the blood pool as dark (‘black blood technique’). This method is mainly used to delineate the anatomic structure of the heart. Fatty infiltration of the myocardium, which is the main feature of ARVC, can identified using this technique+-

- Gradient echo imaging: This is the opposite of spin echo imaging – myocardium appears dark and the blood pool appears bright (‘bright blood technique). This technique is used to evaluate ventricular mass, left and right ventricular cavity sizes and function, valvular function, intracardiac shunts, and also to detect intracardiac masses. Steady state free precession or SSFP is related approach which can generate high spatial (~2mm in-plane) and temporal (<30 millisecond) cine images within an 8 to 12 second breathhold.

- Flow velocity encoding: It is also known as phase contrast technique and it is used to directly quantify the blood flow. It can also be used to quantify the severity of valve regurgitation and stenosis, size of intracardiac shunts and severity of an arterial stenosis.

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Gating

Two types of gating are generally used in cardiac MRI (CMR) – *ECG gating* by monitoring the cardiac cycle and *respiratory gating* by monitoring respiration.

Even though real time CMR methods which acquire the entire image in less than 100 milliseconds are available, this method is limited by low temporal and spatial resolution. Therefore, ECG gating is generally used and data is acquired over multiple cardiac cycles. This gives a better spatial resolution. Good ECG gating methods can provide excellent image quality in sinus rhythm and sometimes even with atrial fibrillation or presence of atrial or ventricular premature beats.

Most of the images can be done during breath holds. However, images which require longer acquisition time can be done only using respiratory gating in addition to cardiac ECG gating. This is mainly useful in high resolution imaging of the coronary arteries. Respiratory gating can either be done by using a navigator to track the movement of the diaphragm or using an elastic band around the chest which can monitor respiratory motion

Safety

Cardiac MRI does not produce any ionizing radiation which may be harmful to patient or caregivers. However, it can be potentially problematic in patients with metallic implants which are ferromagnetic. Therefore, screening of patients prior to MRI imaging is mandatory. Gadolinium based contrast agents can cause nephrogenic systemic fibrosis in patients having renal disease with a glomerular filtration rate of

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less than 30mL/min. But this can be avoided by avoiding contrast MRI in such patients.

MR Planes of Imaging

Important MR views include the true planar or Tru-FISP, 2-chamber view, short axis, long axis, four-chamber view and true two-chamber view. The true planar view may be seen in axial, sagittal or coronal sections. To obtain a two-chamber view, first a true axial scout image is taken through the left ventricle and then an oblique coronal scout view is positioned parallel to the interventricular septum(31).

For obtaining short-axis view, a double oblique image must be prescribed from a true axial image and a two-chamber scout image showing both the left atrium and the left ventricle. The planes of imaging must be along the long axis of the left atrium and the left ventricle on both the images. For obtaining a long-axis left ventricular view, an imaging plane should be positioned from the apex of left ventricle through the mitral valve using a 2-chamber view which shows the mitral valve. The 4-chamber view is obtained by prescribing an imaging plane which is orthogonal to the short-axis (SA) view(31).

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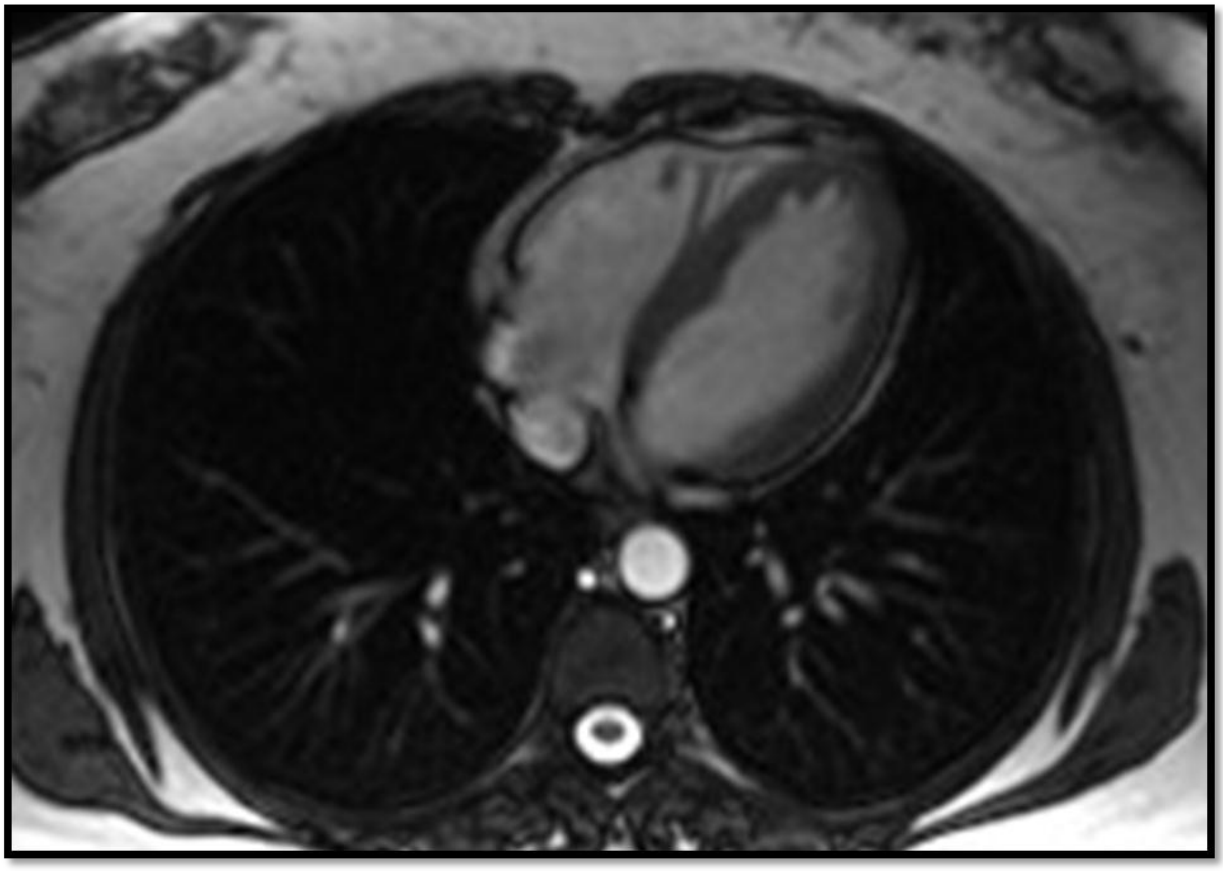
TRUFISP axial sections of the chest at the level of pulmonary artery



TRUFISP axial sections of the chest showing four chamber view

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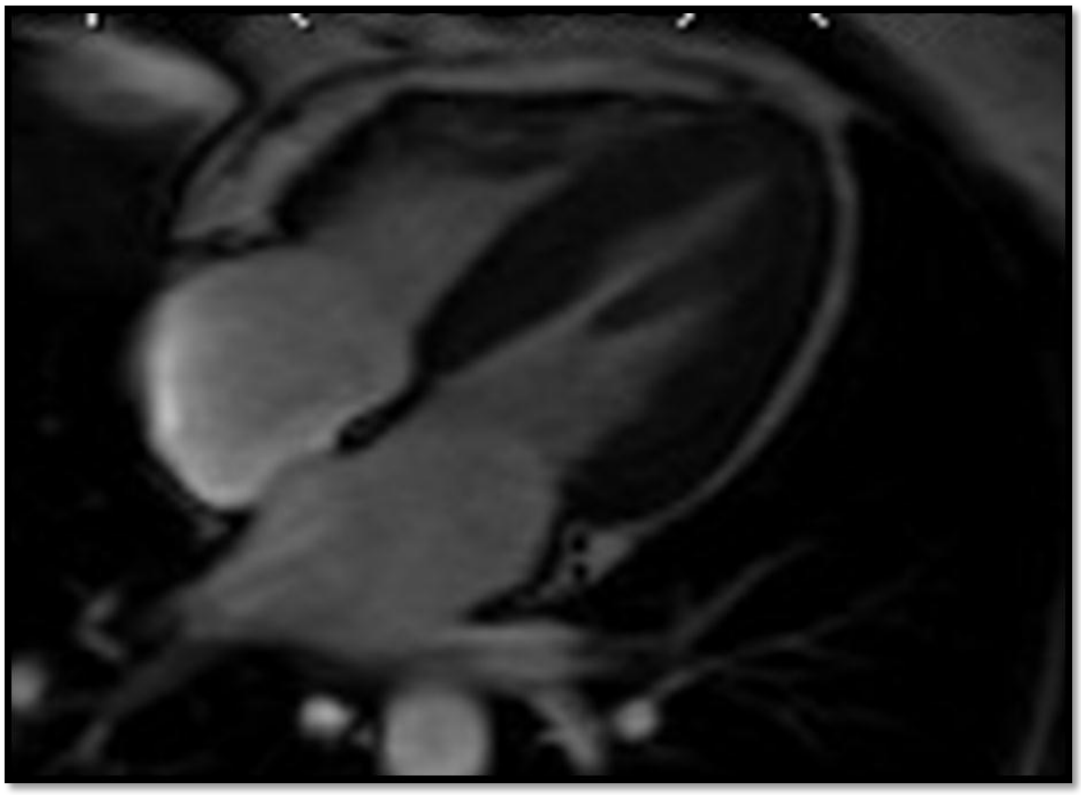
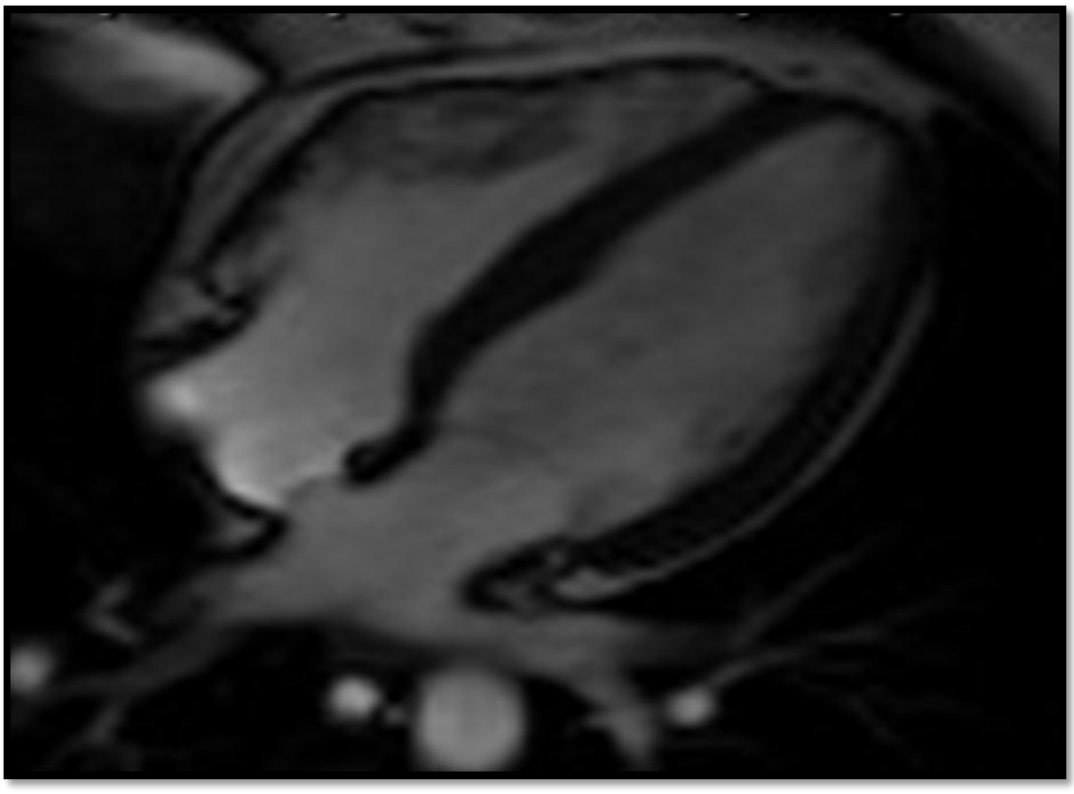


CINE image - four chamber (horizontal long axis) view in systole



CINE image - four chamber (horizontal long axis) view in diastole

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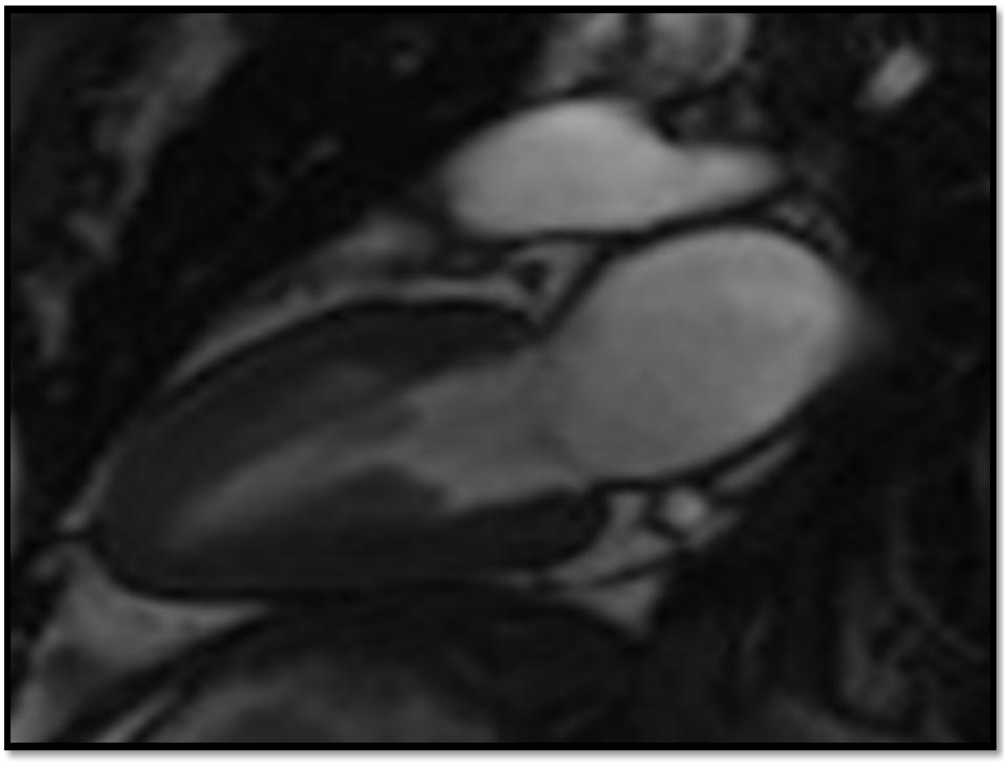
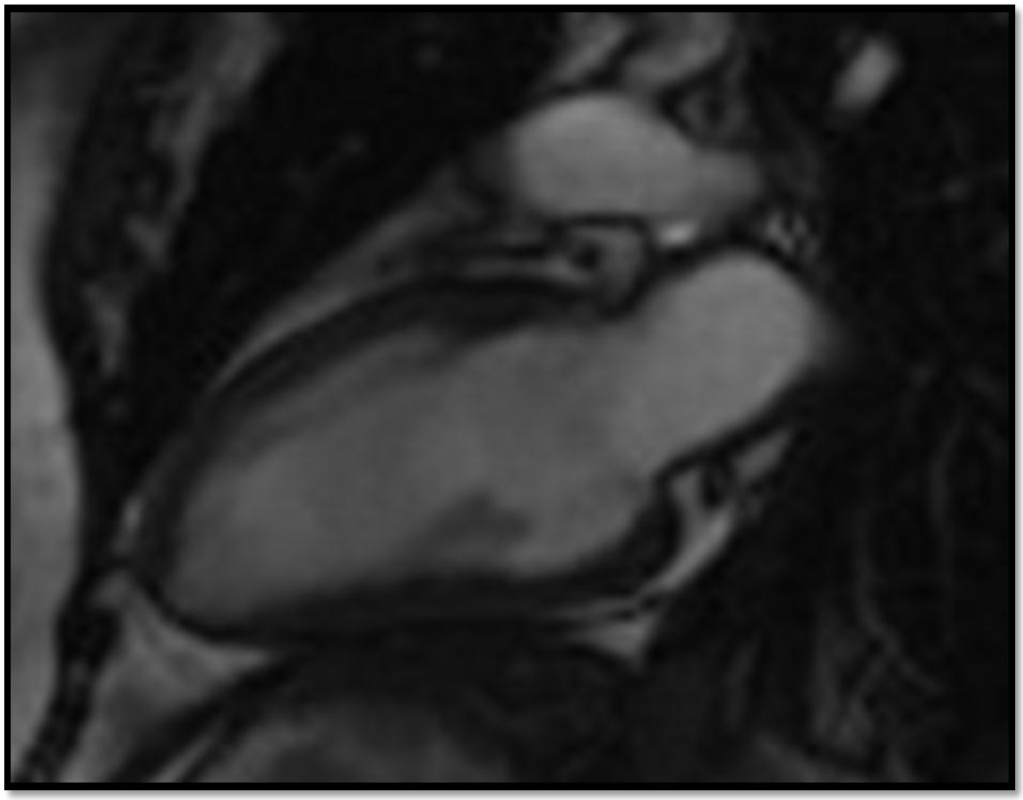


CINE image – 2 chamber view (vertical long axis view) of left ventricle in systole



CINE image - 2 chamber view (vertical long axis view) of left ventricle in diastole

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CINE image - 2 chamber view (vertical long axis view) of right ventricle in systole

CINE image - 2 chamber view (vertical long axis view) of right ventricle in diastole

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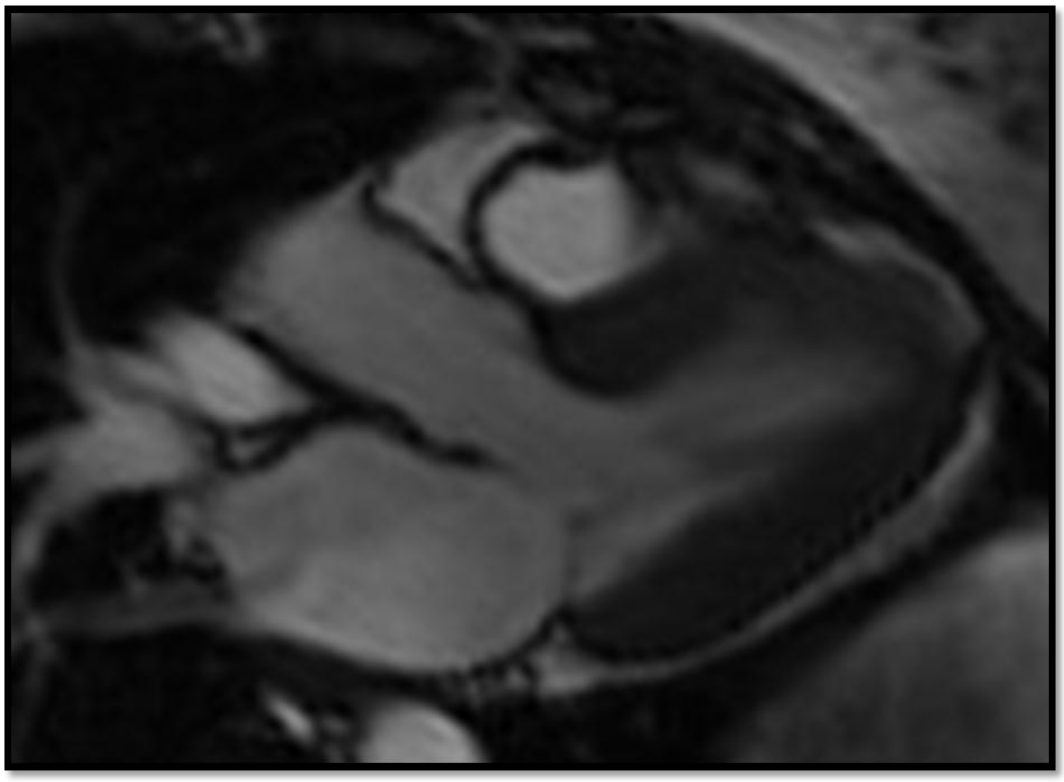
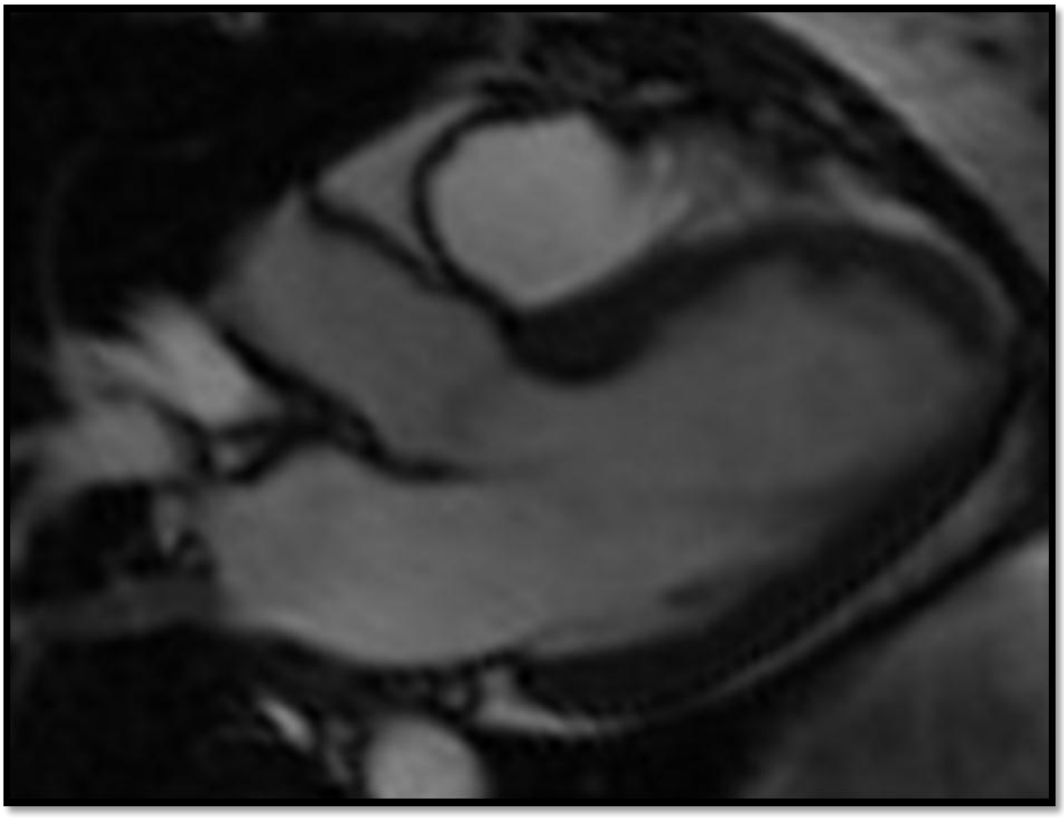


CINE image - left ventricular outflow tract in systole



CINE image - left ventricular outflow tract in diastole

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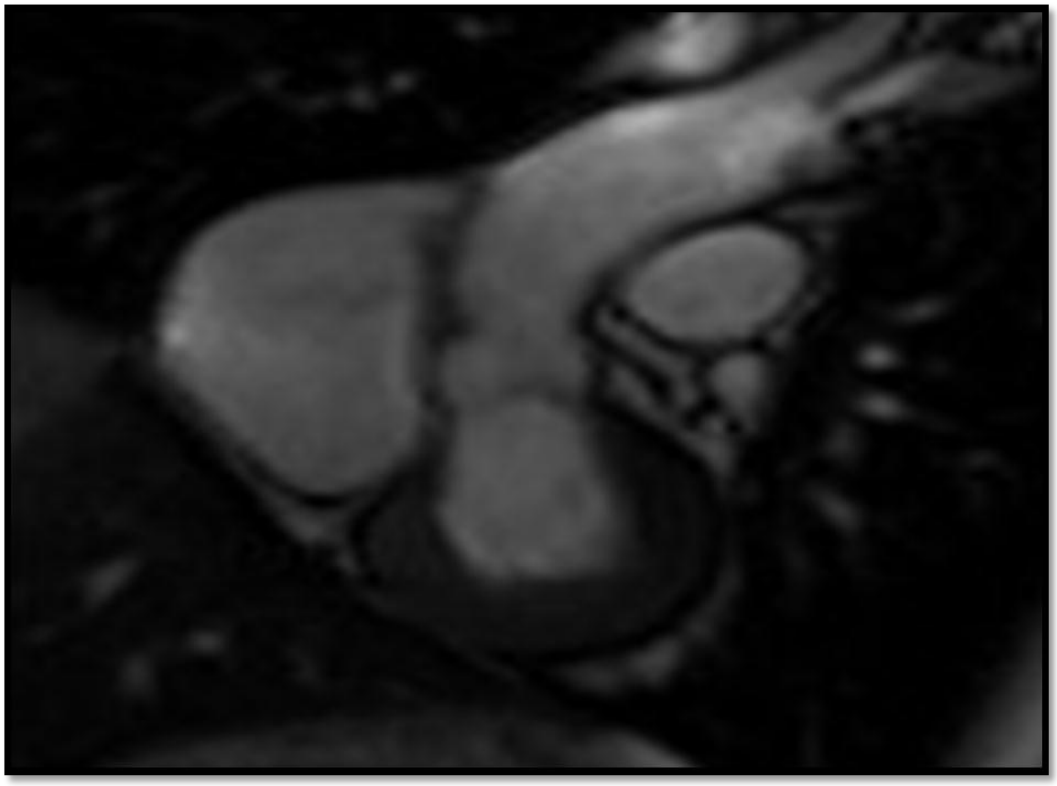
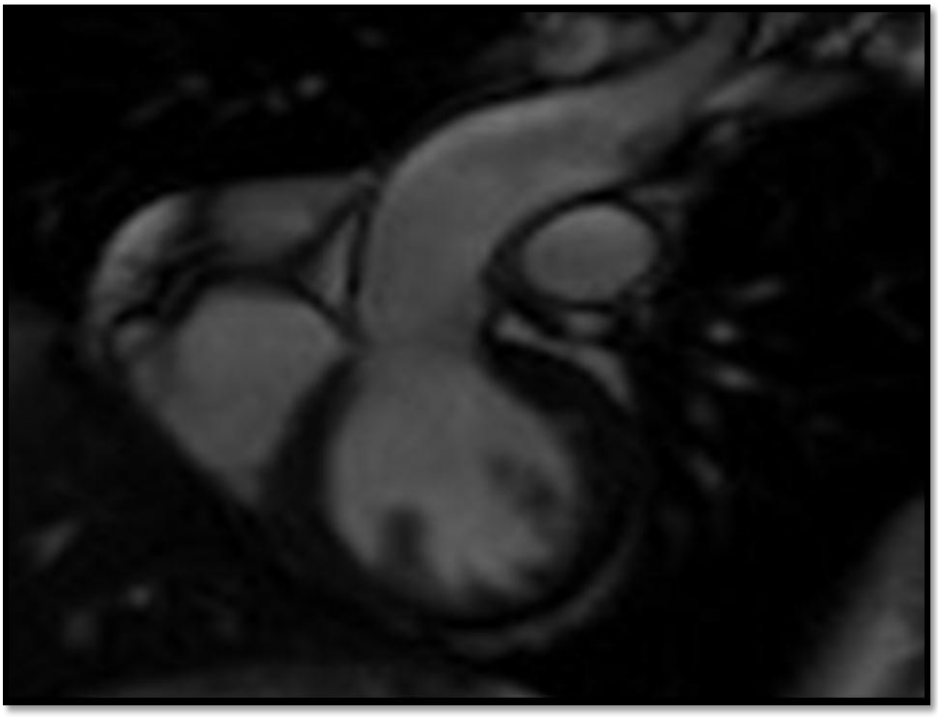


CINE image - left ventricular outflow tract in systole



CINE image - left ventricular outflow tract in diastole

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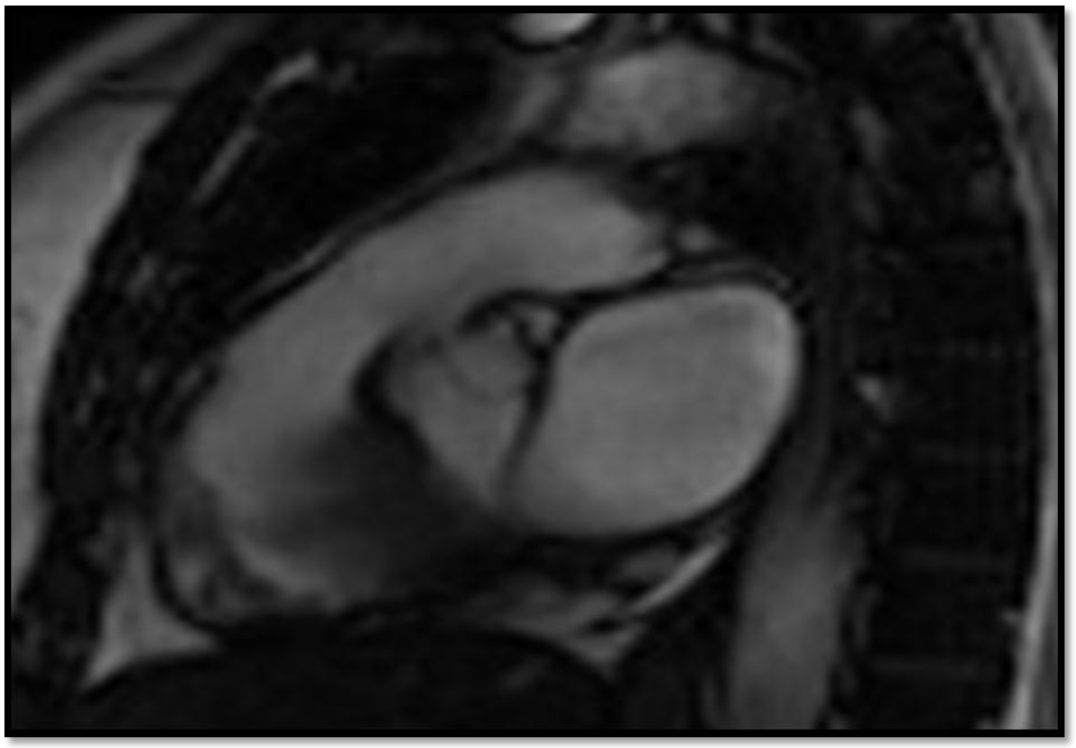
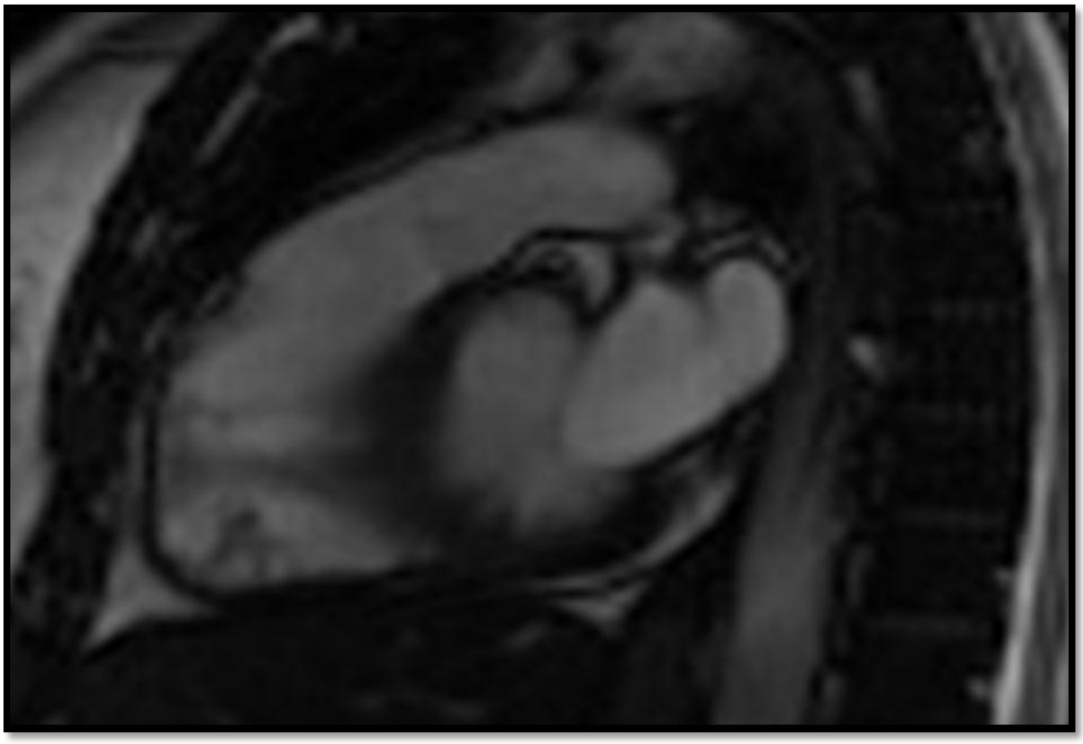


CINE image - right ventricular outflow tract in systole



CINE image - right ventricular outflow tract in diastole

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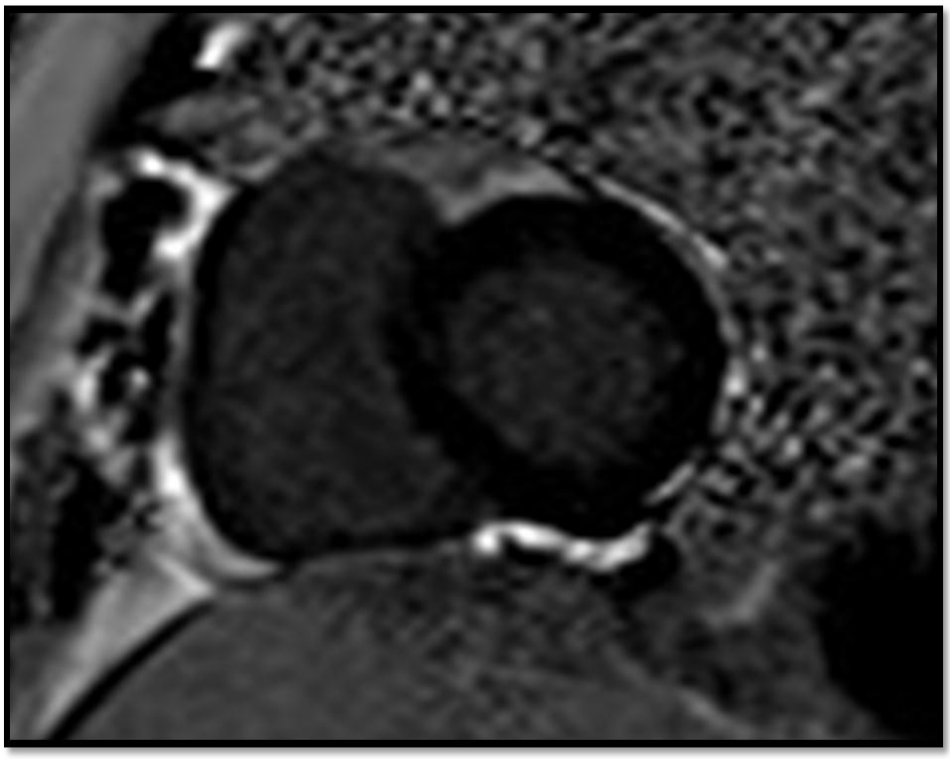
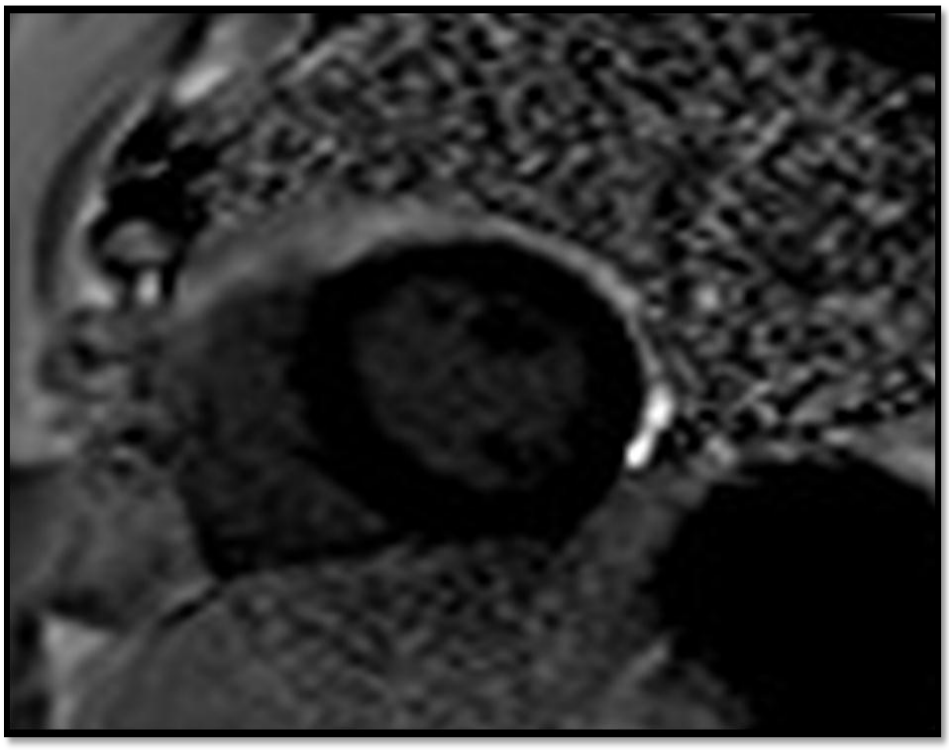


PSIR image - short axis view at the basal level



PSIR image - short axis view at mid cavity level

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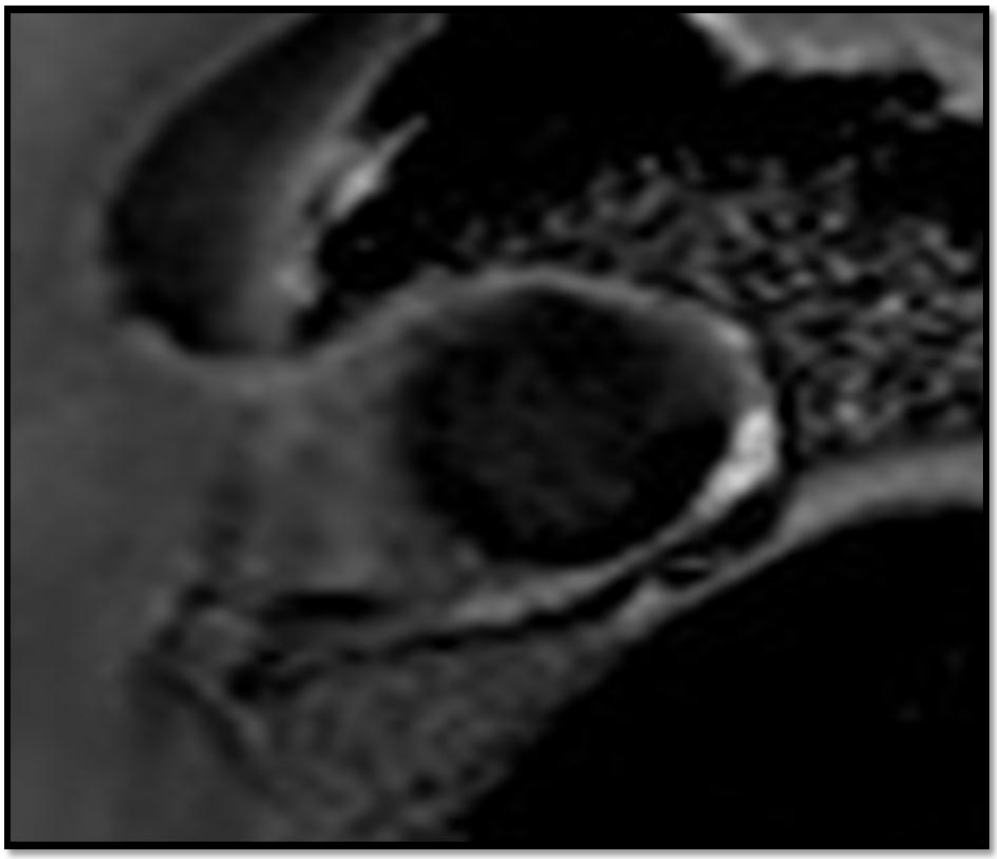
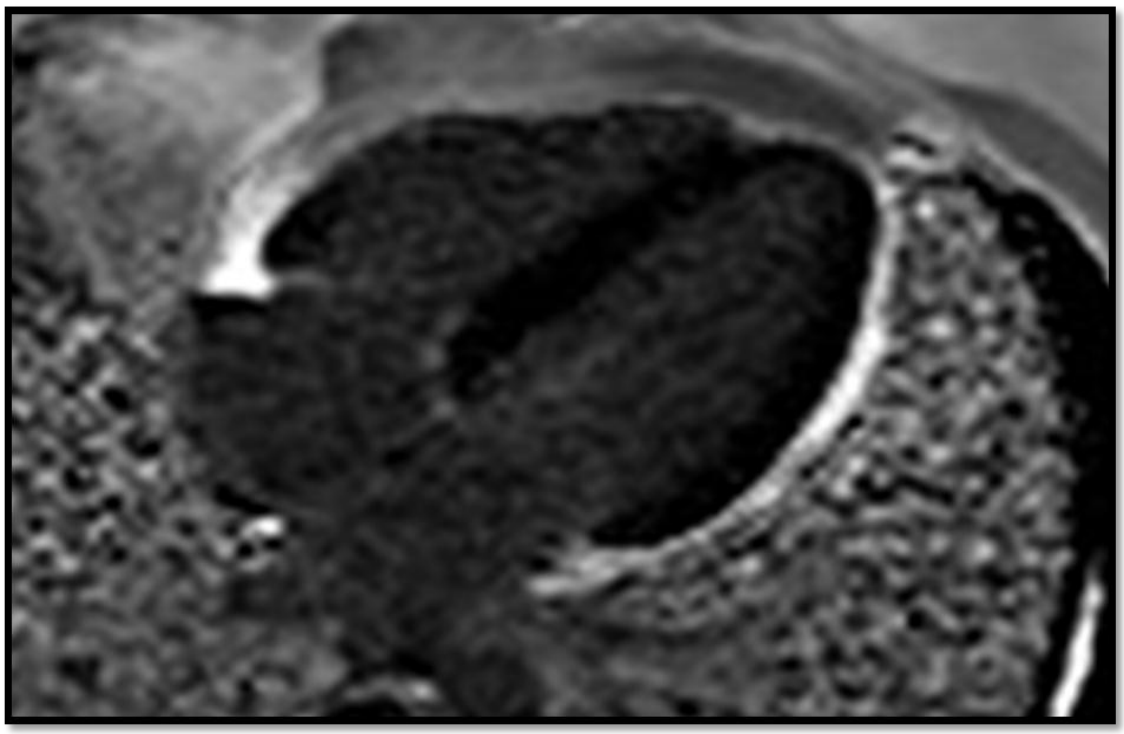


PSIR image - short axis view at apical level



PSIR image – four chamber view

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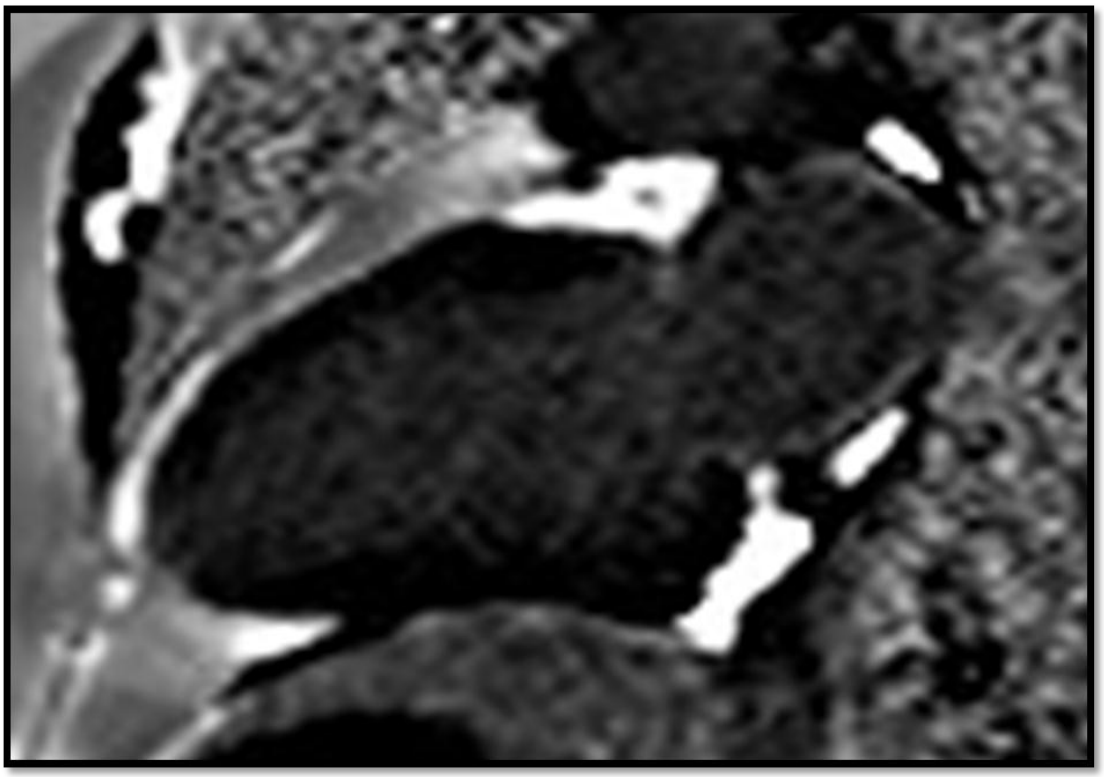

PSIR image - two chamber view of the left ventricle

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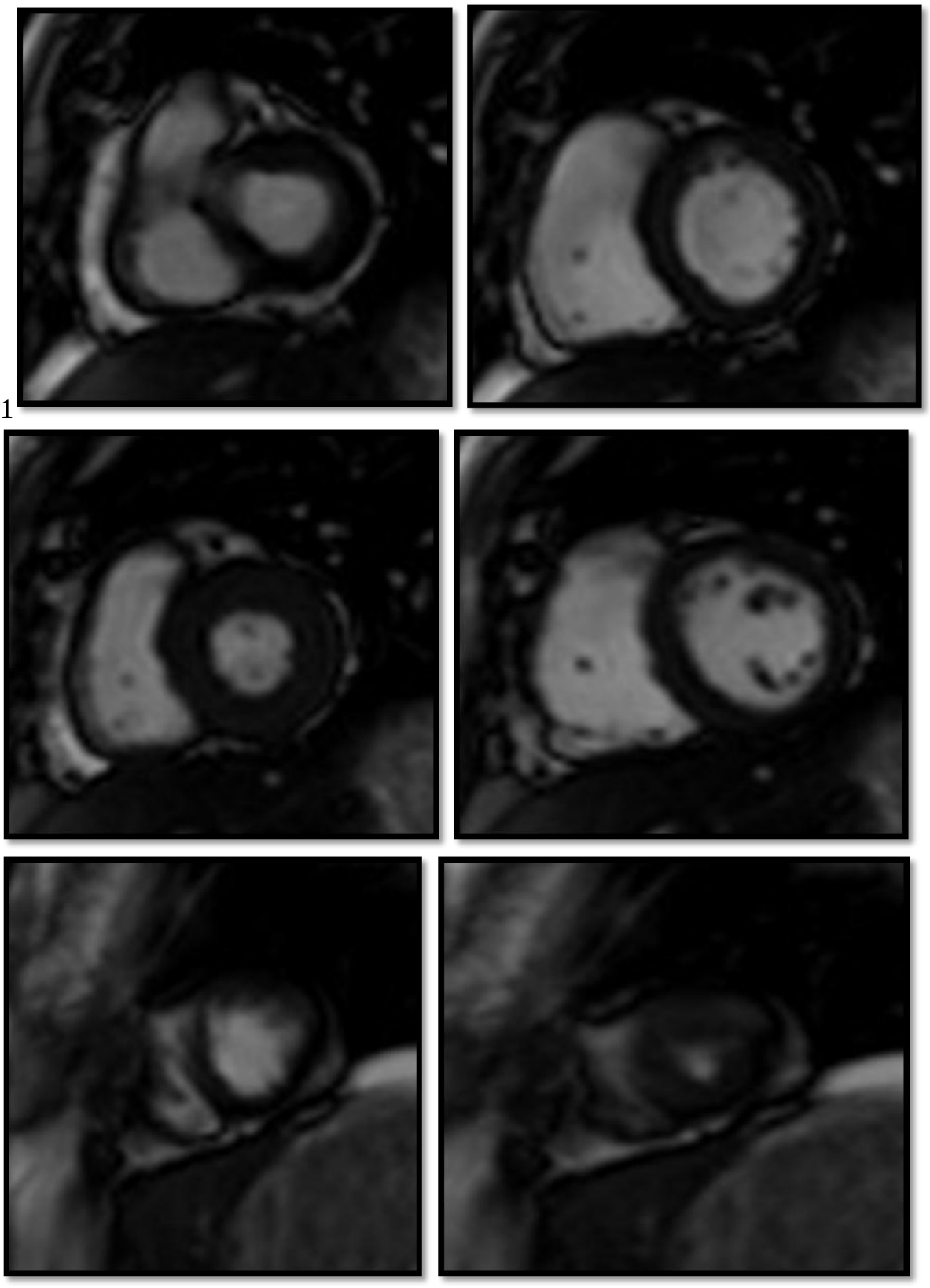

CINE short axis views in systole and diastole at basal, mid-cavity and apical levels

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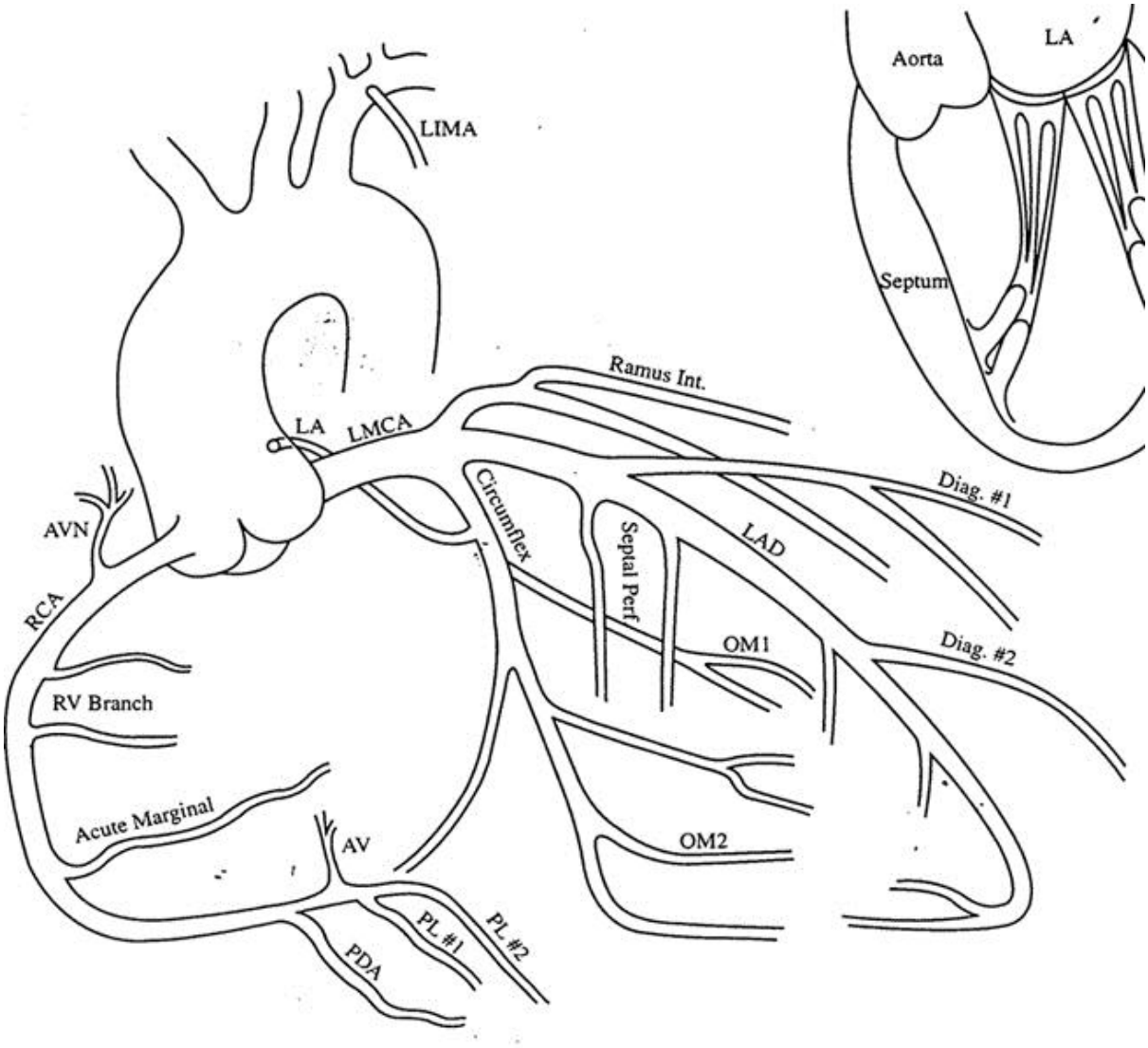
CORONARY ARTERY ANATOMY

The heart is supplied by two main coronary arteries which arise from the aorta and it receives about 5% of the total cardiac output. Blood supply to the heart is more during diastole than during systole unlike in other parts of the body. The coronary blood supply increases by about 3-5 times during exercise.



Courtesy: www.meddean.luc.edu

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There are two major arteries supplying the heart:

- Left main coronary artery (LMCA)
- Right coronary artery (RCA)

Left main coronary artery (LMCA) arises from the left coronary cusp. Its length is variable ranging from 10-15mm and almost immediately divides into the circumflex artery (Cx) and the left anterior descending artery (LAD). Sometimes, it can divide into three branches, the third branch arising between the LAD and Cx known as ramus intermedius which behaves as the diagonal branch of Cx. This variation can be seen in 15% of the normal population.

Left anterior descending artery (LAD) traverses through the anterior interventricular groove upto the apex of the left ventricle. It gives off multiple septal branches which supply the anterior part of the interventricular septum and diagonal branches which mainly supply the anterior wall of the left ventricle. The first diagonal branch (D1) denotes the distinction between proximal and mid portion of LAD. More than one diagonal branch may be seen.

Left circumflex artery (LCx) is located in the left atrio-ventricular groove and supplies the lateral wall of left ventricle through vessels known as obtuse marginal. They supply the lateral margin of the left ventricle and branch off with an obtuse angle. In about 10 to 20% of the population, left dominant circulation is seen in which case the left circumflex artery supplies the posterior descending coronary artery.

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Right coronary artery arises from the right coronary sinus of Valsalva and traverses the right atrio-ventricular groove. The first branch in 50-60% cases is a small conus branch which supplies the RV outflow tract. In 60% cases, a sinus node artery arises as the second branch of RCA which runs posteriorly to the Sino-atrial node (In the rest of the 40%, it originates from the circumflex artery). The next branches are diagonal branches which supply the anterior wall of right ventricle. A large acute marginal branch (AM) comes off at an acute angle and supplies the lateral wall of right ventricle. The RCA continues down to give off a branch to the AV node. 70 to 80 % of the population has right dominant circulation in which the right coronary artery gives off the posterior descending artery which supplies the inferior wall of the left ventricle and inferior part of the septum.

17 SEGMENT MODEL OF THE LEFT VENTRICLE

Myocardial segments showing abnormal enhancement or wall motion abnormality are named and localized according to 17 segment model of the American Heart Association.

Individual myocardial segments of the left ventricle can be assigned to the 3 major coronary arteries supplying the heart taking into consideration that there may be anatomic variability(32).

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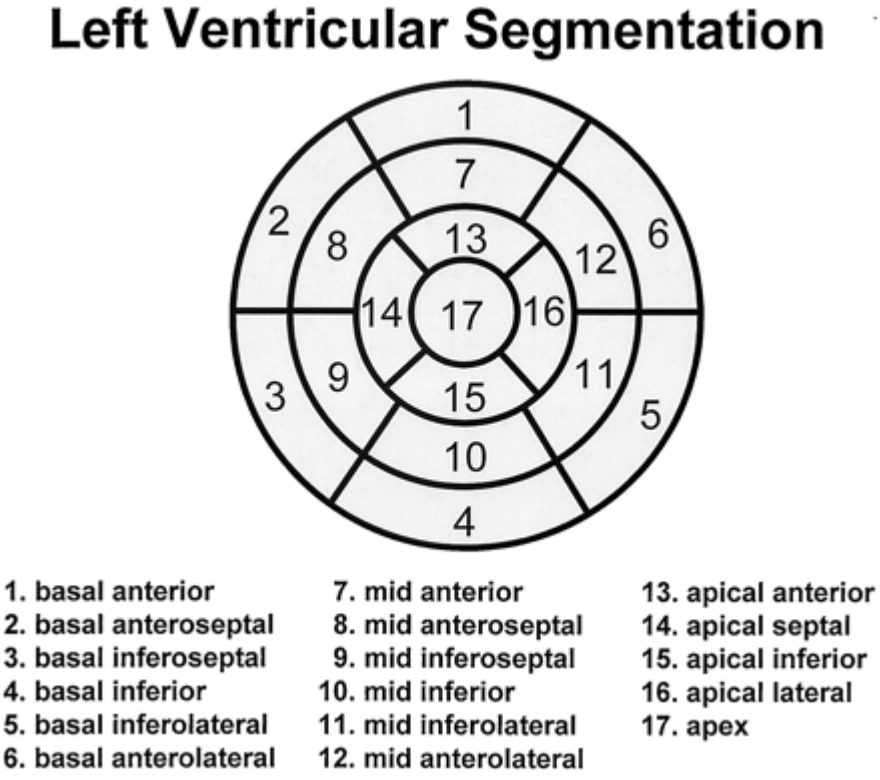

Adapted from: *www.circ.ahajournals.org*

The heart is divided into three sections of equal longitudinal length - basal level, mid-cavity level and apical level. The basal and mid-cavity levels are each divided into six equal segments with each line dividing the segments drawn at 60 degrees angle to one another. The point of attachment of the right ventricular wall to the left ventricle is used to identify and separate the septum from the anterior and inferior free walls of the left ventricle. Apical level is divided into four equal segments. The papillary muscles are anatomical land marks to differentiate between the mid cavity level from the basal and apical levels. The apex is the 17^{th} segment which is defined by the absence of cavity. It is the muscular tip of the left ventricle. The apex is seen on the long axis images.

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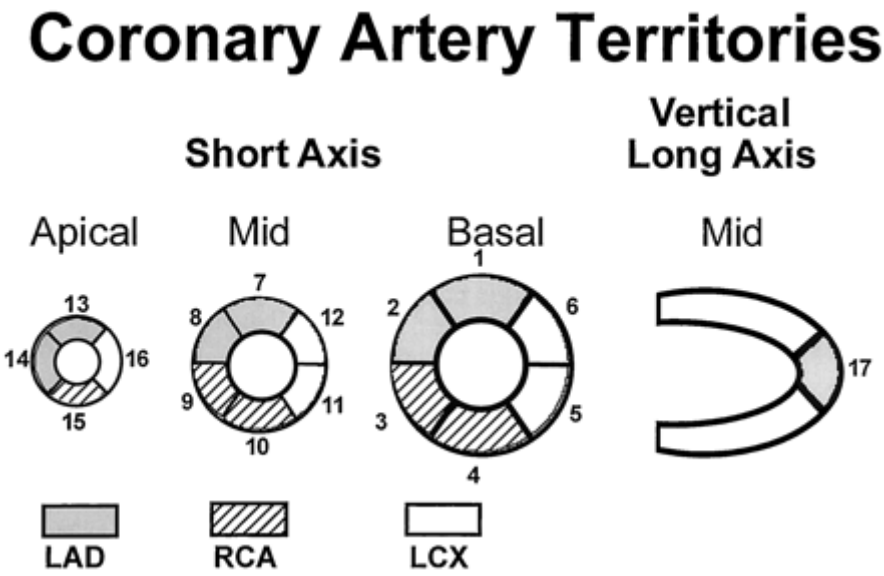

From:www.circ.ahajournals.org

Even though there is tremendous variability in the coronary blood supply, each segment of the 17 segment model has been assigned to one of the three major coronary arteries. This is used for assessing the regional wall motion abnormalities, perfusion defects and delayed enhancement patterns.

WHY DO STRESS CARDIAC MRI

Stress cardiac MRI offers the greatest information from a single test and can be a one stop shop for evaluation of patients with suspected coronary artery disease as it is non-invasive and provides high resolution images of the heart in any desired plane and without radiation.

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Adenosine ‘‘stress’’ MR myocardial perfusion imaging has a proven high sensitivity and negative predictive value for the detection of myocardial ischemia(33)(34)(35)(36)(37)(38)(39)(40)(41)(42)(43)(44).

High diagnostic accuracies are reached in patient groups with relatively high prevalence of disease in studies combining rest-stress perfusion and delayed contrast enhancement.

In low risk patients, stress MRI perfusion study if performed may reduce the number of purely diagnostic Coronary angiographies (CAG’s), which would be important because CAG is an invasive test with a risk of complications and relatively expensive.

In a recent study done by Lubbers et al, the diagnostic capability of ‘‘stress-only’’ perfusion cardiac MR was assessed using adenosine for detection of ischemia so that it can be used as an indicator for doing CAG in patients with no a past history of MI. Adenosine stress perfusion alone was done in 139 patients. 14 out of them (10.1%) had a perfusion defect suggestive of ischemia. Concurrent CAG on the same 14 patients showed full agreement with the stress perfusion scans.(45)

In another recent study, it was noted that major adverse cardiac events (MACE) risk was very low (<1% in a year) in patients with normal adenosine stress MR. MACE in this study were defined as nonfatal MI, death due to a cardiac cause, and revascularization with PCI or CABG surgery.(46)

A non-invasive technique can thus be used to determine which patients need to undergo coronary angiography.

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Safety of MRI and Contrast agent

Once cleared to have an MRI scan, there are no risks from the MRI machine as such. A very small risk (0.1%) exists of allergic reaction to the contrast medium injection (Gadolinium).

Nephrogenic systemic fibrosis is a rare but significant side effect of contrast injection that manifest in weeks to months as a side effect of contrast injection in patients with poor kidney function or those already on dialysis, however these patients are not included in the study

Other than claustrophobia or foreign bodies such as aneurysmal clips, there are no contraindications for MRI.

Safety of adenosine

Bernhardt et al in 2006 studied the side effects of adenosine stress MRI in 3,174 patients. 35% patients reported minor complications like dyspnoea or mild chest pain (in 30%), asymptomatic and temporary AV block (in 3%) and nausea (in 2%). These effects resolve rapidly upon termination of the infusion, as the half-life of adenosine is very short (in seconds). Aminophylline can be used as an antidote, but it is seldom necessary. Adenosine is thus an extremely safe pharmacologic stress agent.

Pharmacology of adenosine

Adenosine has some essential functions in human physiology. It is a ubiquitous extracellular signaling molecule with effects on multiple organ systems but an

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important role in the cardiovascular system. It is an endogenously occurring purine nucleoside composed of an adenine molecule attached via a beta-N9-glycosidic bond to a ribose sugar moiety (‘ribofuranose’).

It is catabolized rapidly by the enzyme adenosine deaminase into inosine. The drug ‘dipyridamole’ exerts its action by inhibition of the enzyme adenosine deaminase’.

Adenosine has 4 types of receptors which it binds to: A1, A2A, A2B and A3 (47). It has the highest affinity for A1 and A2a receptors. A2A and A2B receptor activation produces significant vasodilation in most vessels including the coronaries, resulting in an increase in myocardial blood flow. A1 receptors have generally an inhibitory action on most tissues. A1 receptor activation mediates inhibition of the AV node, prolongation of the refractory period and also results in a myocardial depressant effect with negative dromotropic and chronotropic effects.

Activation of A2A receptors also has anti-inflammatory effects and this acts as a target of caffeine. Human mast cells have A2B receptors and this is thought to produce mast cell degranulation and bronchial constriction.

It is the activation of A2A receptors and the resultant increase in myocardial blood flow that makes it possible for the use of adenosine for stress testing.(48)

Route of administration:

Central venous administration of adenosine was thought to the Gold standard for induction of coronary hyperemia, especially for the assessment of Fractional Flow Reserve (FFR). However, studies by De Bruyne et al and others have shown that both

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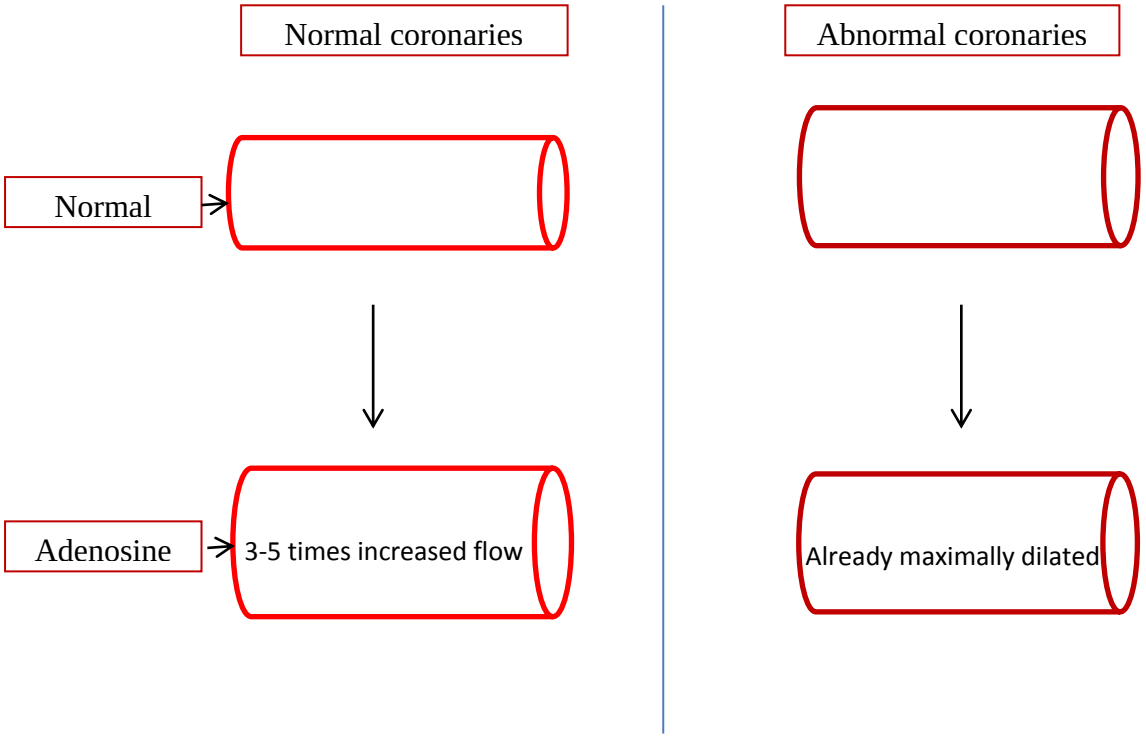
central and peripheral infusions have similar hyperemic efficacy. They also found that increase the dose more than 140ug/kg/min did not increase the vasodilator action of adenosine further. (49)

Effect on coronaries

In healthy coronary arteries, the vasodilator response results in a four- to fivefold increase in coronary blood flow after a standard adenosine infusion protocol. The typical haemodynamic response includes a slight reduction in both the systolic and diastolic blood pressures and a mild increase in the heart rate as a result of induced peripheral vasodilatation.



Adenosine is a potent coronary vasodilator.

In patients without CAD, the resistance vessel blood flow is increased significantly to almost 3-5 times above the baseline.

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In patients with CAD and having significant stenosis in the proximal coronary artery, the resistance vessels distal to the hemodynamically significant stenosis are usually maximally dilated in order to maintain the normal resting flow. Hence, the blood flow through these vessels and consequently into the myocardium supplied by these vessels is not affected by adenosine.

In short, adenosine will induce a “steal phenomenon” wherein more blood flows into the normal coronaries. This results in a perfusion defect in the areas supplied by the abnormal coronaries. This mechanism of action of adenosine is used for assessment of myocardial ischemia wherein under the effects of adenosine, the ischemic myocardium stands out as a perfusion defect in MRI.

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MATERIALS AND METHODOLOGY

STUDY PERIOD: The study was conducted in the Department of Radiology and Cardiology in the period between March 2014 and May 2015.

RECRUITMENT:

Inclusion criteria: Patients with suspected/diagnosed coronary artery disease, who are advised to undergo adenosine stress MRI in the period between March 2014 and May 2015.

Consecutive patients who were advised to undergo adenosine cardiac MRI stress testing based on their clinical history, ECG and ECHO findings and/or coronary angiogram were informed about the cardiac adenosine stress MRI scan and the project in detail.

If the patient volunteered to have the adenosine cardiac stress MRI, assuming that he/she does not have any known contraindication for the same, they would be enrolled in the study.

The cost was arranged by the patient themselves when affordable. If they were unable to afford the scan, provision for the scan was arranged for them through the grant for the research project.

INFORMED CONSENT: Informed consent (enclosed) was taken by the principal investigator.

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DATA COLLECTION:

1. Demographic details of the patient were collected. Relevant data like history of risk factors (age, sex, hypertension, dyslipidemia, diabetes mellitus, past history of MI, past history of stenting and CABG) were recorded.
2. Reporting of echocardiography and coronary angiogram were done by the co – investigator cardiologist of the concerned unit.
3. The adenosine cardiac MRI stress scan was performed in the MRI room of our Radiology department with a Siemens 1.5 T MRI machine and the scan was reported by the principal investigator in a standardized format and checked by a radiologist of professor grade (Guide)
4. The ECHO and coronary angiography of a recruited patient was interpreted and reported by the co-investigator of the same unit under which the patient was being treated in.

INTERPRETATION OF CARDIAC MRI:

5. 17 cardiac segment model as described by the American Heart Association was used in the description of the extent of stress and rest perfusion defect, delayed hyperenhancement and wall motion abnormality or any other lesion that may be identified
6. An area of pure ischemia will show up as a stress perfusion defect in the absence of rest perfusion defect or delayed hyperenhancement.

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An area of ischemia along with infarction will show up as a larger stress perfusion defect along with a smaller rest perfusion defect and with a delayed hyperenhancement.

An area of infarct will show up as a regional wall motion abnormality with hyperenhancement on delayed scans along with stress and rest perfusion defects.

Adenosine is coronary vasodilator which causes stress perfusion defects in ischemic segments by the ’steal phenomenon’

7. Left ventricular function: The LV ejection fraction was calculated by the Siemens 1.5 T MRI machine specific software which is dedicated software provided by the same company. The software used is Argus software (Siemens, Erlangen Germany AG) .This software is already validated, being used widely internationally and is approved by the SCMR (Society for Cardiac Magnetic Resonance Imaging)
   The software allows us to outline the endocardium in multiple planes of short axis view of both the ventricles at end diastole and end systole. The machine then generates the ejection fraction, stroke volume and cardiac output from this.
8. Regional wall motion abnormality(RWMA) was assessed by visual eyeballing
9. Stress ischemic defect due to hypoperfusion along a coronary artery territory appears dark on stress perfusion scans but appears normal on rest perfusion and delayed hyperenhancement scans.

   Infarcted areas appear dark on both stress and rest perfusion scans and bright on delayed hyperenhancement scans.

`

Artefacts appear as defects (“dark”) which do not persist in all the images in a series and they do not conform to a specific coronary artery territory.

Coronary Artery Condition	**Distal Flow**	**Perfusion stress**	**Perfusion rest**	**Delayed hyperenhancement**
Normal	Normal	Without defects	Without defects	*“All black”*
Stenosis (ischemia)	Normal at rest (maximally dilated)	*With defects*	Without defects	*“All black”*
Stenosis (infarction)	Absent	*With defects*	*With defects*	*Bright signal*
Artefact	Normal	*With defects which are not persistent*	*With defects which are not persistent*	*Bright or dark*
Ischemia +Infarction	Reduced	*With larger defects*	*With defects*	*Bright signal*

`

10. Delayed enhancement pattern was scored as:

0 – 0% Hyperenhancement in a RWMA

1 - Hyperenhancement of 1 to 25% thickness of the wall in a myocardium with RWMA

2 - Hyperenhancement of 26 to 50% thickness of the wall in a myocardium with RWMA

3 - Hyperenhancement of 51 to 75% thickness of the wall in a myocardium with RWMA

4 - Hyperenhancement of 76 to 100% thickness of the wall in a myocardium with RWMA

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STATISTICAL ANALYSIS

Statistical analysis was done using SPSS software

RESULTS AND ANALYSIS:

A total of 84 patients underwent adenosine stress cardiac MRI study. Of these, coronary angiogram was performed for 26 patients.

DEMOGRAPHY

A. AGE:

The mean age of the study population was 55 years. The average age for males was 56 years and that for females was 54 years. Majority of the population (69%) belonged to the age group between 50 to 70 years. 22.6 % of the population was in the age group of 40 to 50 years. 4.8% and 3.6% of the patients were in the age group of 30 to 40 years and more than 70 years respectively.

{Fig.1, Table. 1}

Age group (years)	Numbers	Percentages
30-40	4	4.8
40-50	19	22.6
50-60	29	34.5
60-70	29	34.5
>70	3	3.6
TOTAL	84	100

Table 1 – age distribution of study population

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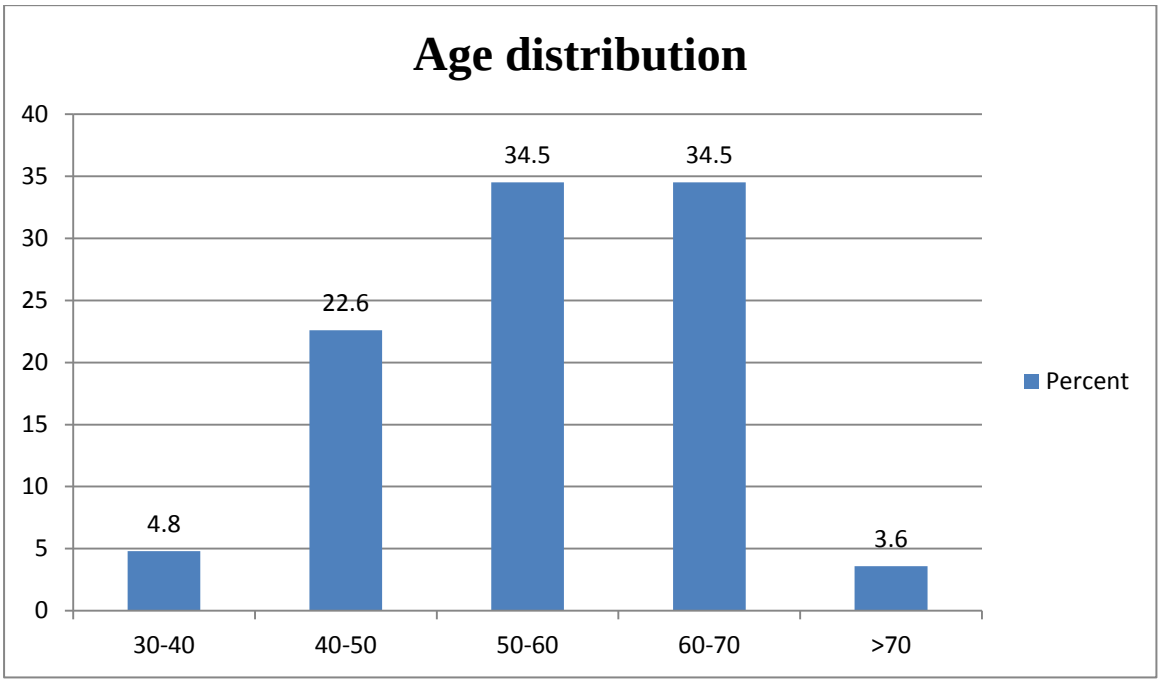

Fig.1 - age distribution graph

B. GENDER: 72.6% (61) of the population were males. Only 27.4 % (23) of the population were females.

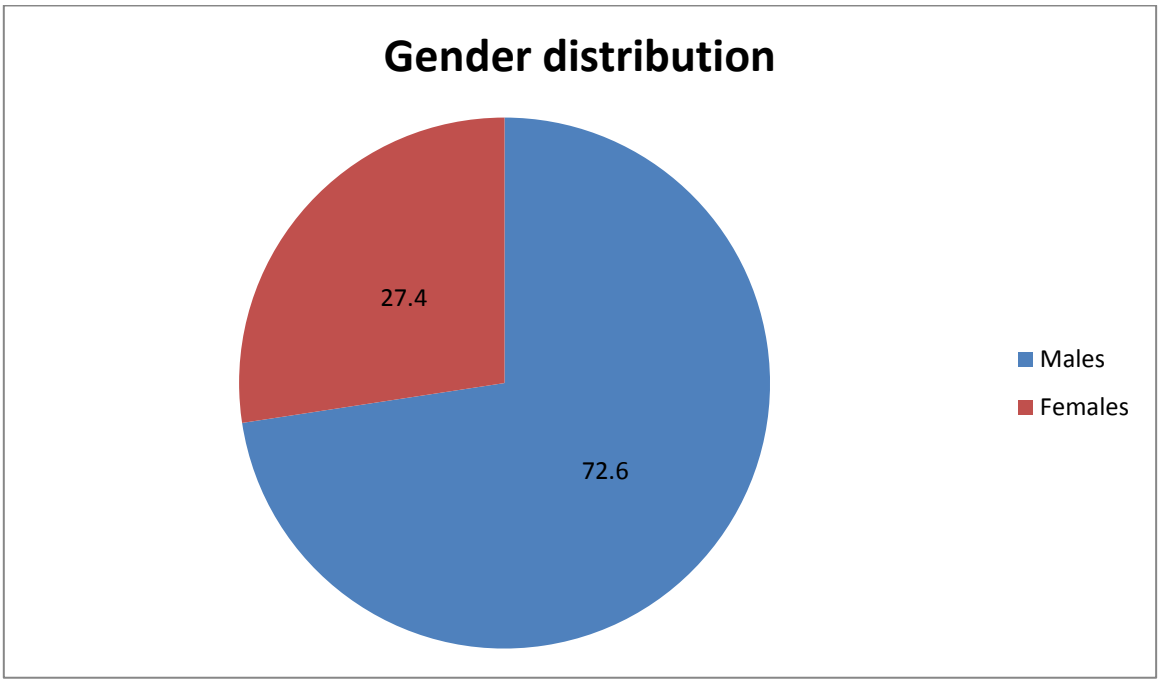

Fig. 2 – Genderwise distribution of the study population

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CLINICAL FEATURES

A. DIABETES MELLITUS: 35.7% of the study population had diabetes mellitus and 64.3% were non diabetic. {Table 2 – presence of diabetes in study population}

Diabetic?	Frequency	Percent
yes	30	35.7
no	54	64.3
Total	84	100.0

Table 2 – presence of diabetes

B. HYPERTENSION: 52.4 % of the population were non-hypertensives while 47.6% were hypertensives. {Table 3 – history of hypertension in the study population}

Hypertensive?	Frequency	Percent
yes	40	47.6
no	44	52.4
Total	84	100.0

Table 3 – presence of hypertension

C. DYSLIPIDEMIA: Majority (66.7 %) of the study population had no dyslipidemia while 33.3% only had dyslipidemia {Table 4 – history of dyslipidemia in study population}

Dyslipidemic?	Frequency	Percent
yes	28	33.3
no	36	66.7
Total	84	100.0

Table 4 – presence of dyslipidemia

`

D. PAST HISTORY OF MYOCARDIAL INFARCTION: 64.3%(54) of the population had no past history of myocardial infarction while 35.7%(30) had previous myocardial infarction. {Fig.3, Table 5 – past history of MI}

Past h/o MI?	Frequency	Percent
yes	30	35.7
no	54	64.3
Total	84	100.0

Table 5 – past history of myocardial infarction

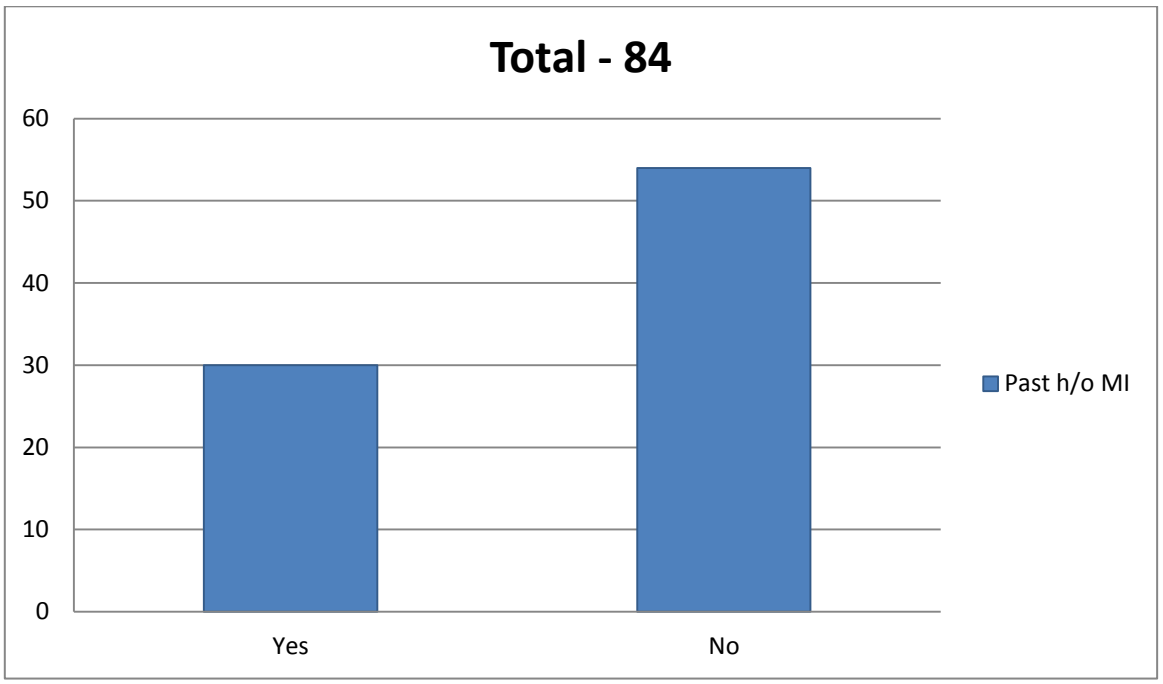

Fig.3 – past history of MI in the study population

E. PAST HISTORY OF ANGIOPLASTY / STENTING: Only 5 patients (6%) had an angioplasty or stenting done in the past while the majority (79 patients – 94%) had no previous such history. {Table 6 – past history of angioplasty/stenting}

`

Past h/o plasty/stenting?	Frequency	Percent
yes	5	6
no	79	94
Total	84	100.0

Table 6 – past history of angioplasty/stenting

F. PAST HISTORY OF CABG: Only 2 (2.4%) of the 84 patients had past history of CABG surgery.

FINDINGS ON CARDIAC MRI

A. INDICATION FOR CARDIAC MRI: Majority of the patients (52 patients – 62%) had adenosine stress cardiac MRI done are those with suspected coronary artery disease without having had a history of acute coronary syndrome(ACS) in the past. 32 (38%) patients were those with suspected ischemia with a past history of ACS. {Fig. 4 – indication for stress cardiac MRI}

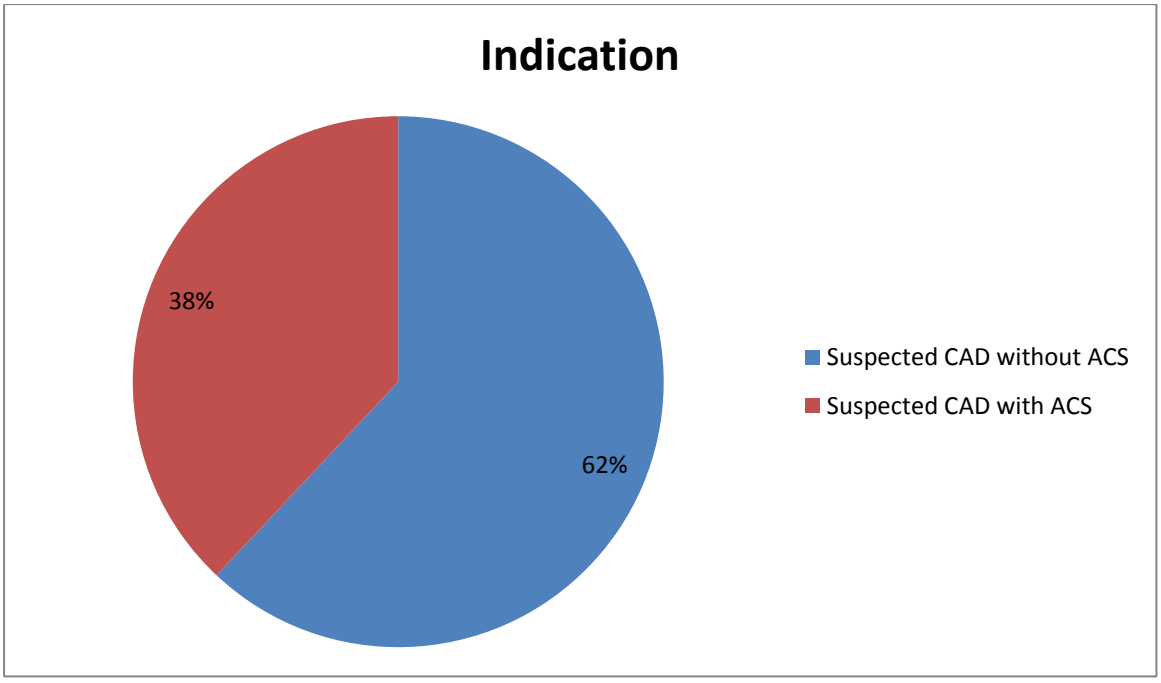

Fig. 4 – Indication for stress cardiac MRI

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B. PRESENCE OF MYOCARDIAL ISCHEMIA: Of the total 84 patients who underwent adenosine stress test, 16(19%) patients were detected to have perfusion defects seen only during stress perfusion scan. The rest of the 68(81%) patients had no evidence of myocardial ischemia. The stress positive cases included those which showed perfusion defects in stress perfusion scans alone (pure myocardial ischemia) and also those which had a larger perfusion defect as compared to the area of delayed enhancement (indicating ischemia with infarction). {Fig.5, Table 7 – presence of myocardial ischemia}

		Frequency	Percent
	yes	16	19
	no	68	81
	Total	84	100.0

Table 7 – presence of myocardial ischemia

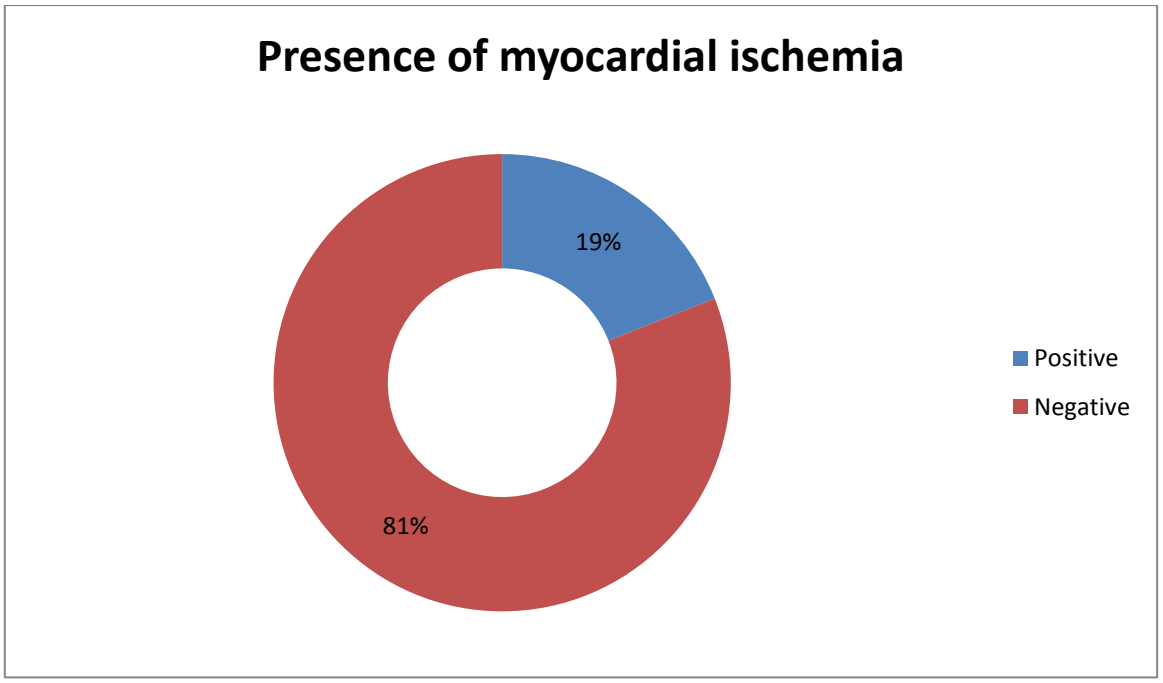

Fig. 5 – presence of myocardial ischemia

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C. ISCHEMIA TERRITORY: 7 out of the 16 patients (44%) had ischemia in the LAD territory. 2 (12.5%) each had ischemia in LCx and RCA territories respectively. 4 patients (25%) had in both LAD and RCA territories. 1 patient (6%) had ischemia in all three vascular territories. {Fig. 6, Table 8 – Territorial distribution of myocardial ischemia}

Ischemia territory	Frequency	Percent
LAD	7	44
RCA	2	12.5
LCx	2	12.5
LAD, RCA	4	25
LAD, LCx	0	0
RCA, LCx	0	0
LAD, RCA, LCx	1	6
TOTAL	16	100

Table 8 – Territorial distribution of myocardial ischemia

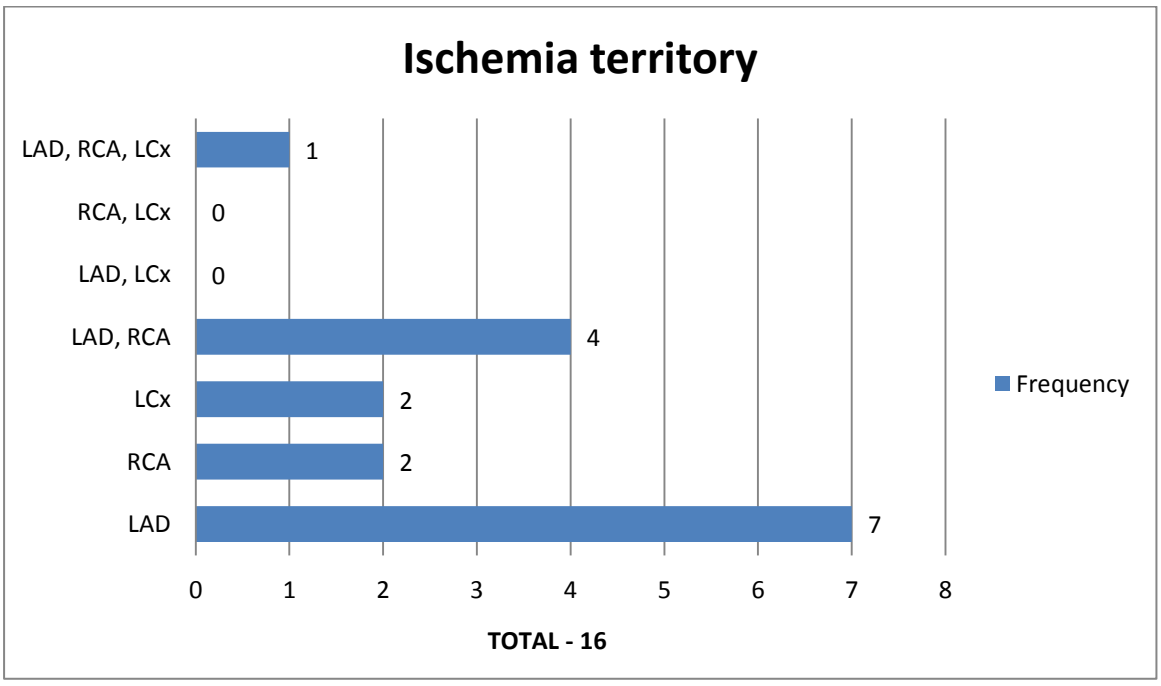

Fig. 6 – Territorial distribution of myocardial ischemia

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D. PRESENCE OF ARTEFACTS: 18 patients (21%) showed artefacts during the perfusion scans. Artefacts include those perfusion defects seen in both stress and rest perfusion scans. 66 patients (79%) had no artefacts in their MRI scan. {Fig.7 – presence of artefacts in MRI}

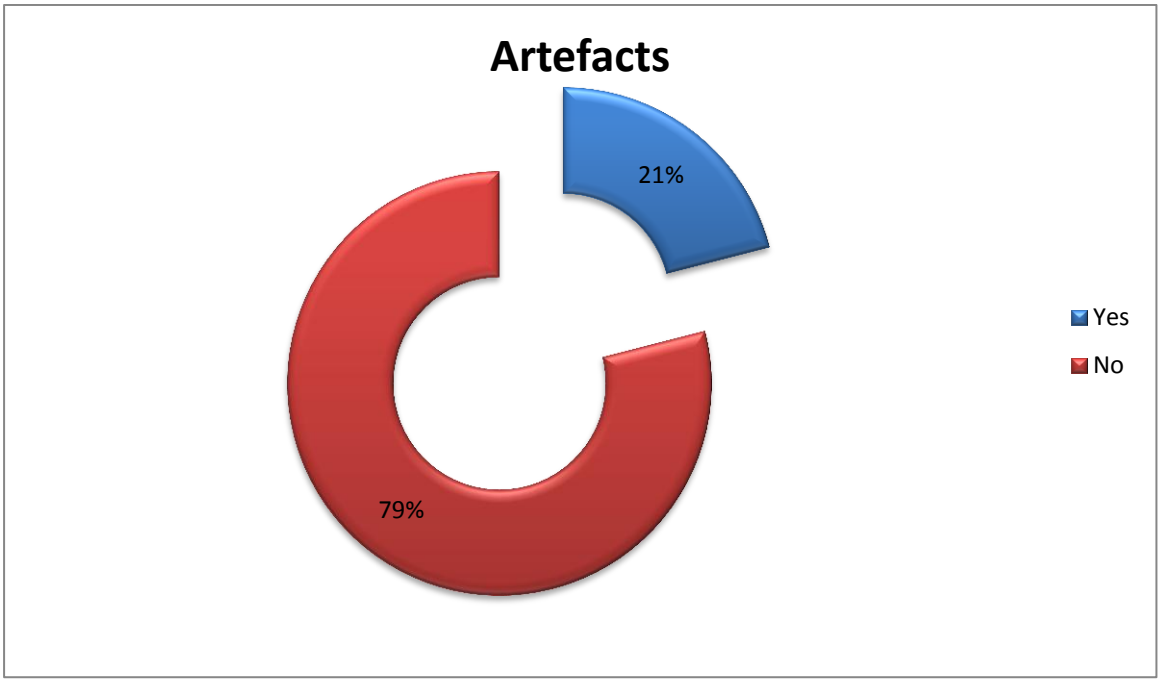

Fig. 7 – presence of artefacts

E. TERRITORIAL DISTRIBUTION OF ARTEFACTS: Out of the 18 patients who showed artefacts on MRI, most (12 patients – 67%) were noted in the LAD territory. The second most common territory was LCx with 3 patients (17%). {Fig.8, Table 9 – territorial distribution of artefacts}

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Artefact territory	Frequency	Percent
LAD	12	66.7
RCA	1	5.6
LCx	3	16.7
LAD, RCA	0	0
LAD, LCx	1	5.6
RCA, LCx	0	0
LAD, RCA, LCx	1	5.6
TOTAL	18	100

Table 9 – artefact territory

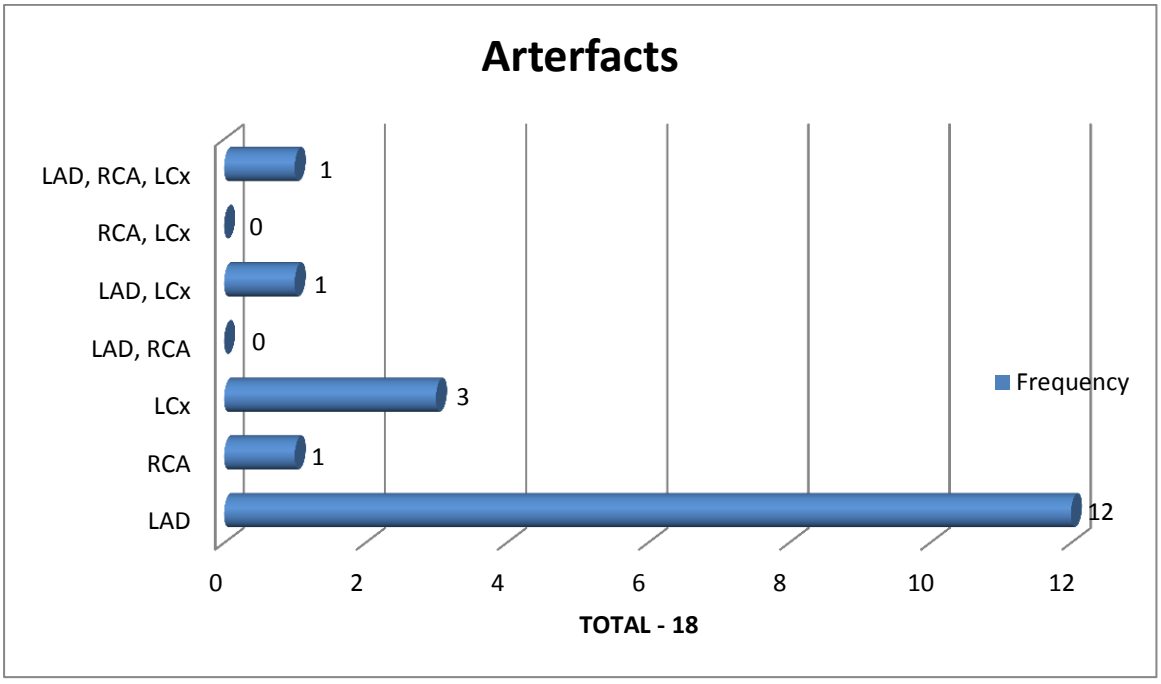

Fig. 8 – Territorial distribution of artefacts

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F. PRESENCE OF DELAYED ENHANCEMENT: 44 patients (52%) showed delayed enhancement while 40 patients (48%) showed no evidence of delayed enhancement. The areas showing delayed enhancement indicate presence of myocardial infarction. {Fig.9, Table.10 – presence of delayed enhancement}

Presence of delayed enhancement	Frequency	Percent
Yes	44	52
No	40	48

Table.10 – presence of delayed enhancement

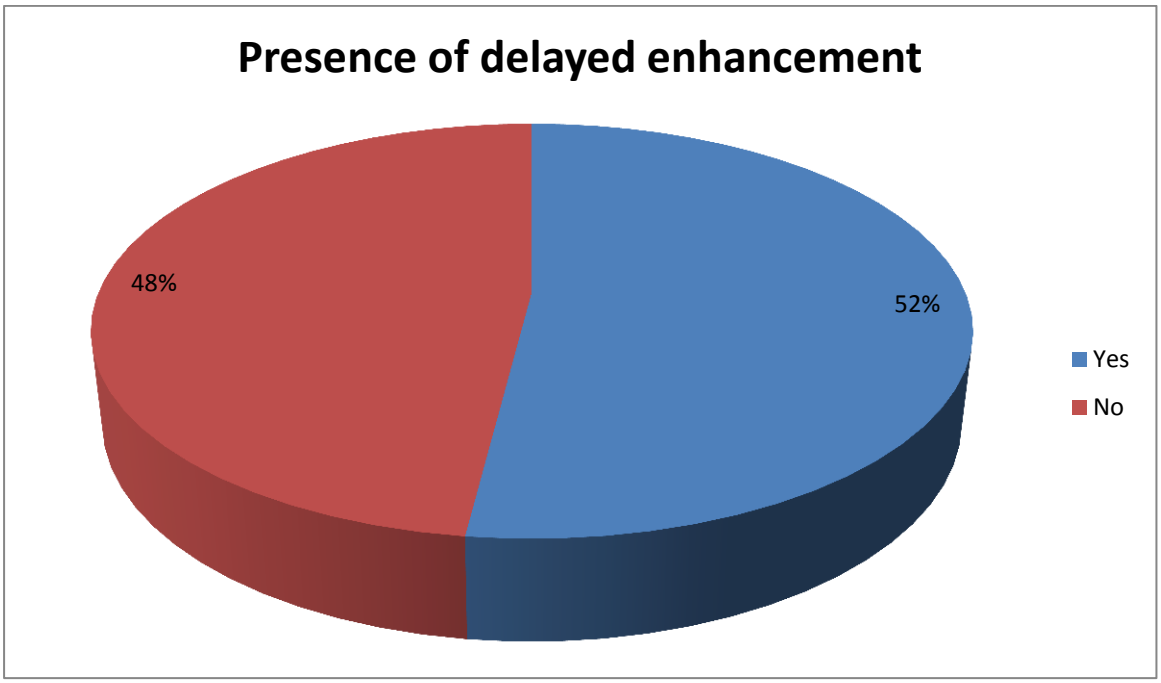

Fig.9 – presence of delayed enhancement

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G. TERRITORIAL DISTRIBUTION OF DELAYED ENHANCEMENT: Out of the 44 patients with presence of delayed enhancement, 25 (56.8%) were noted purely in the LAD territory. This was followed by 6 each (13.6%) in RCA territory and in both LAD and RCA territories. 3 patients (6.8%) had in both LAD and LCx territories. 4 patients (9.1 %) had involvement of all three territories. {Fig.10, Table.11 – Territory wise distribution of delayed enhancement}

Delayed enhancement territory	Frequency	Percent
LAD	25	56.8
RCA	6	13.6
LCx	0	0
LAD, RCA	6	13.6
LAD, LCx	3	6.8
RCA, LCx	0	0
LAD, RCA, LCx	4	9.1
TOTAL	44	100

Table.11 – Territory wise distribution of delayed enhancement

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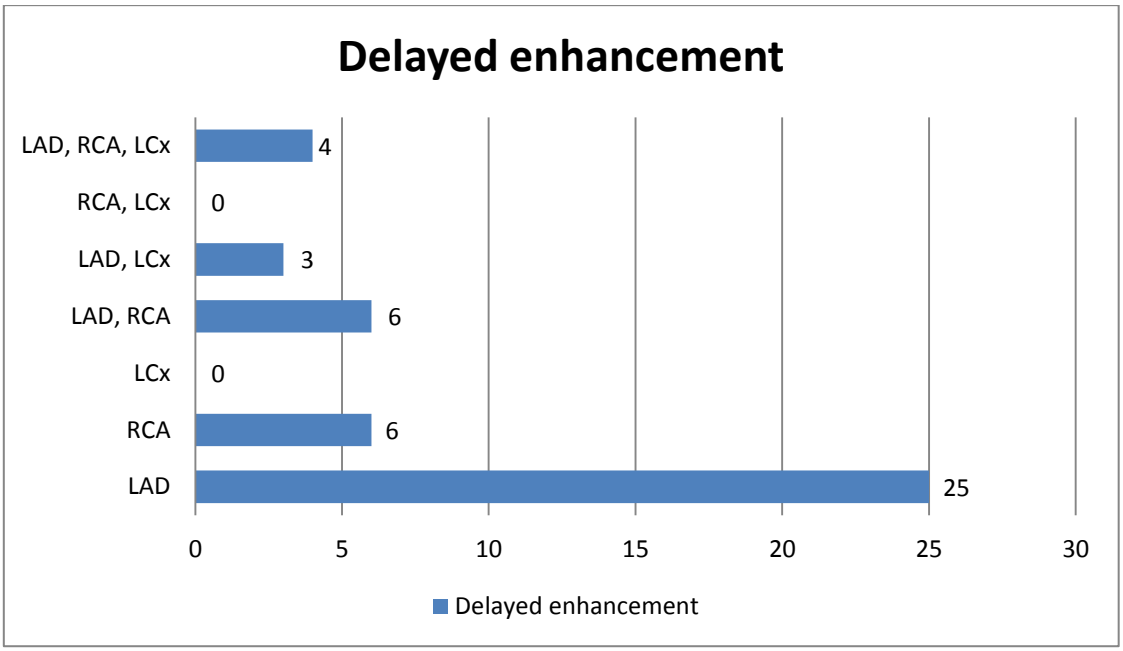
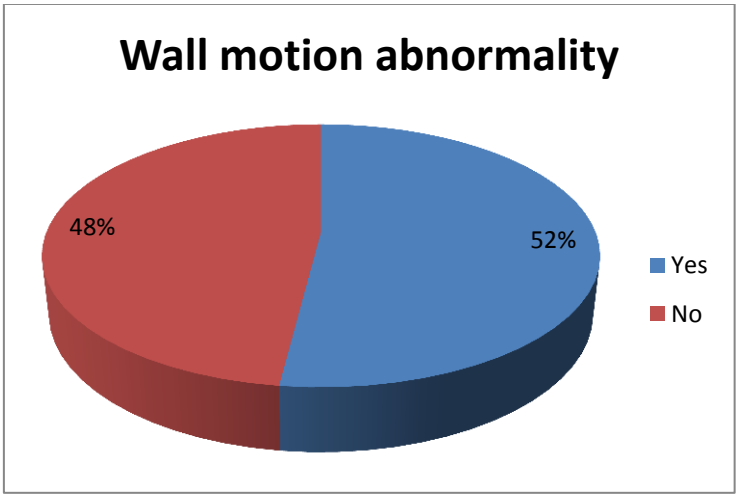


Fig.10 – Territory wise distribution of delayed enhancement

H. WALL MOTION ABNORMALITY: 44 patients (52%) showed delayed enhancement while 40 patients (48%) showed no wall motion abnormalities. {Fig.11, Table.12 – presence of wall motion abnormality}

Presence of wall motion abnormality	Frequency	Percent
Yes	44	52
No	40	48

Table 12, Fig.11 – wall motion abnormality



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I. TERRITORIAL DISTRIBUTION OF WALL MOTION ABNORMALITY:

Out of the 44 patients with wall motion abnormality, 25 (56.8%) were noted purely in the LAD territory. This was followed by 6 each (13.6%) in RCA territory and in both LAD and RCA territories. 3 patients (6.8%) had in both LAD and LCx territories. 4 patients (9.1 %) had involvement of all three territories. {Fig.10 – Territory wise distribution of wall motion abnormality}

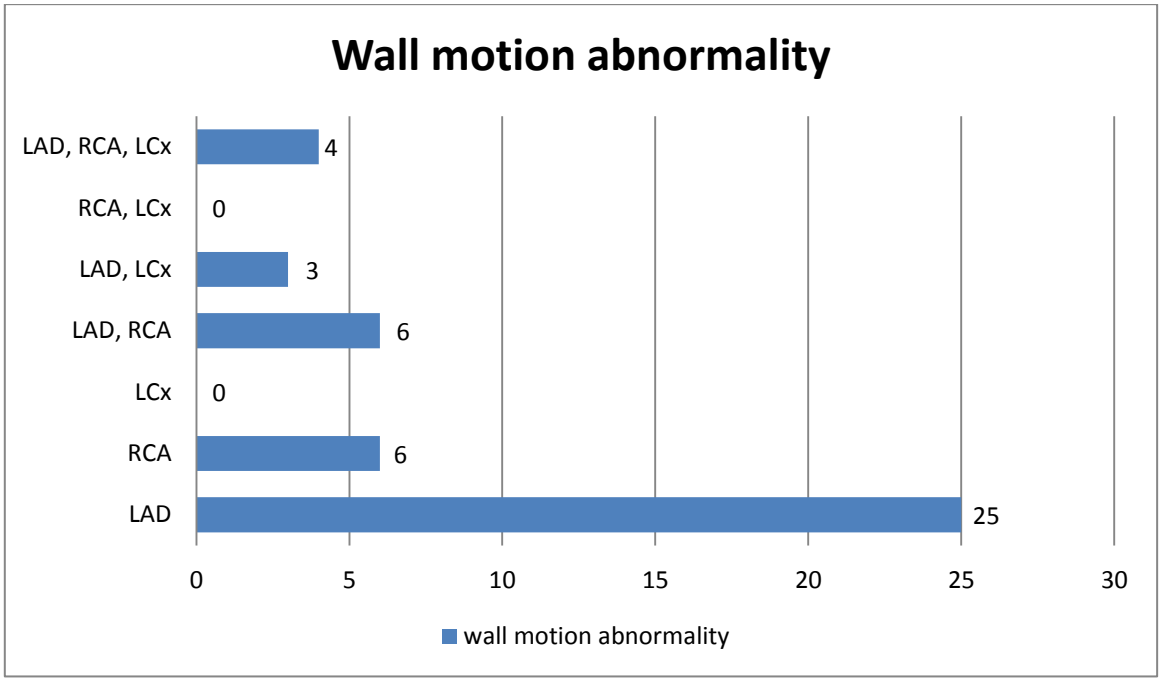

Fig.13 – Territory wise distribution of wall motion abnormality

J. LEFT VENTRICULAR EJECTION FRACTION: The ejection fraction(EF) calculated using short axis cine images from base to apex of the left ventricle with the help of ARGUS software in Philips Synco. {Fig.13, Table.13 – Left ventricular ejection fraction calculated using MRI}

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Mean	50.36
Std. Deviation	17.482
Range	71
Minimum	11
Maximum	82

Table13 -Ejection fraction calculated using MRI

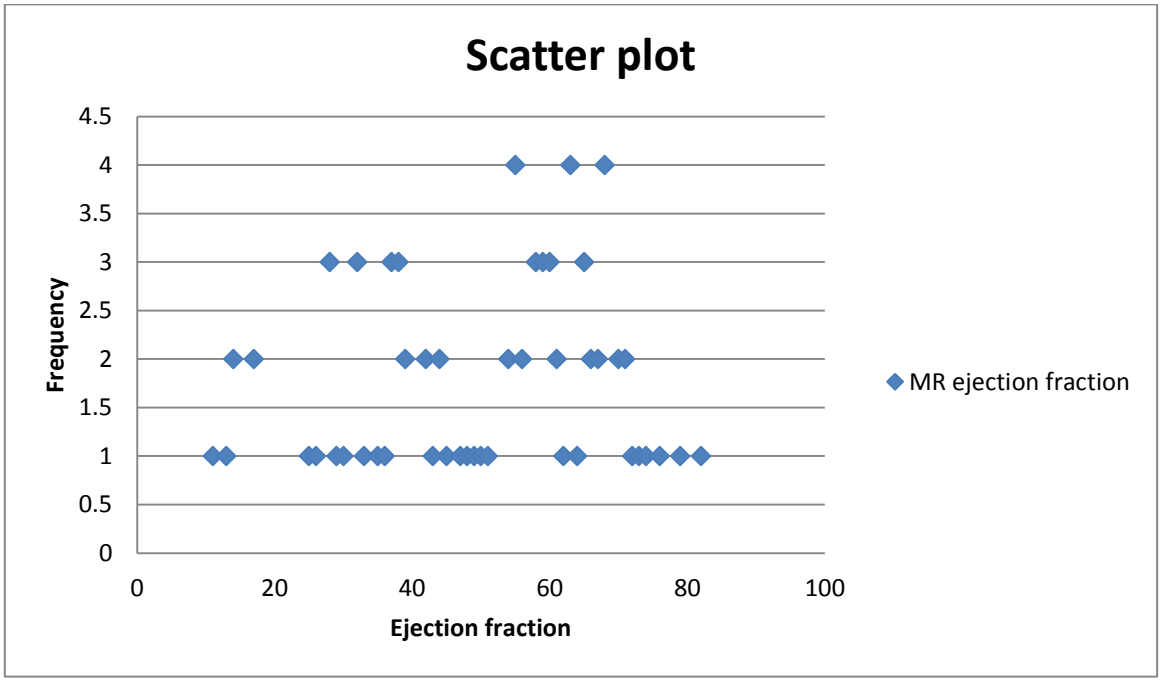

Fig.13 – Scatter plot of ejection fraction calculated using MRI

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FINDINGS ON CORONARY ANGIOGRAM

Invasive coronary angiogram was performed on 25 patients.

A. TYPE OF CORONARY ARTERY DISEASE: Out of the 25 patients who had angiogram done, 9 (36%) had single vessel disease, 8 (32%) had double vessel disease and 7 (28%) had triple vessel disease. 1 patient (4%) had a normal angiogram. {Fig.14, Table.14 – Type of CAD}

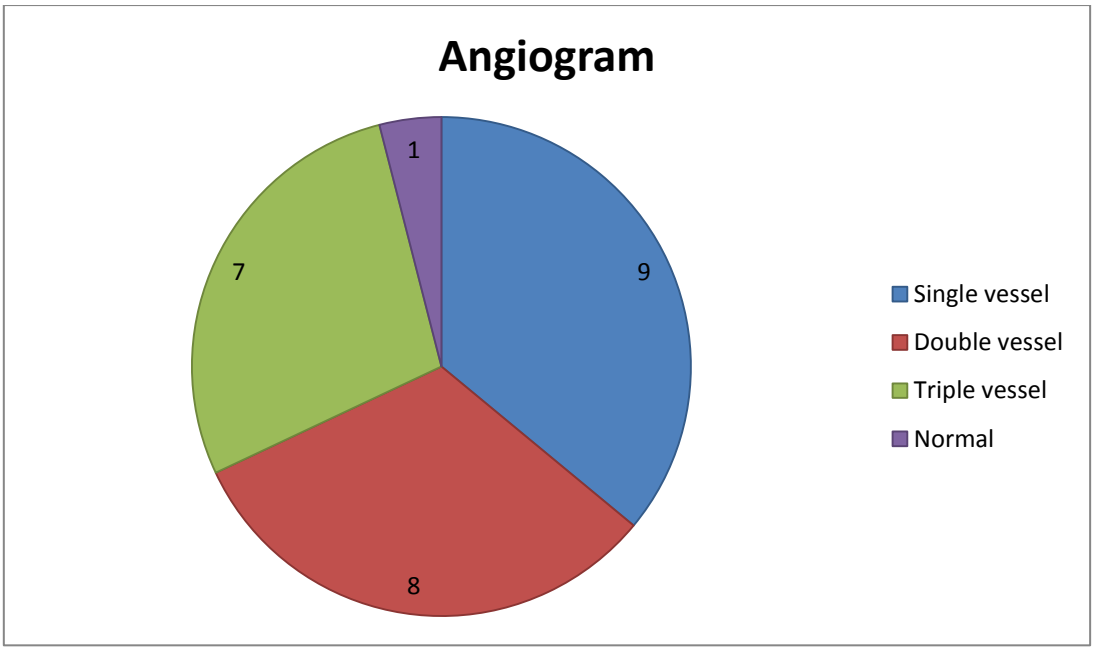

Fig.14 – type of CAD

Type of CAD	Frequency	Percent
Single vessel	9	36
Double vessel	8	32
Triple vessel	7	28
Normal	1	4
Total	**25**	**100**

Table.14 – Type of CAD

`

B. INVOLVEMENT OF LEFT ANTERIOR DESCENDING ARTERY(LAD):

Out of the 25 LADs which were assessed, 24 were diseased while one was normal. Of the diseased LADs, 19 showed significant stenosis of more than 70%, 4 showed 50-70% stenosis and 1 showed minor disease with <50% stenosis. {Fig.15, Table.15 – Involvement of LAD}

Percentage of stenosis	*Frequency*	*Percent*
<50%	1	4
50-70%	4	16
>70%	19	76
Normal	1	4
Total	**25**	**100**

Table 15 – Involvement of LAD

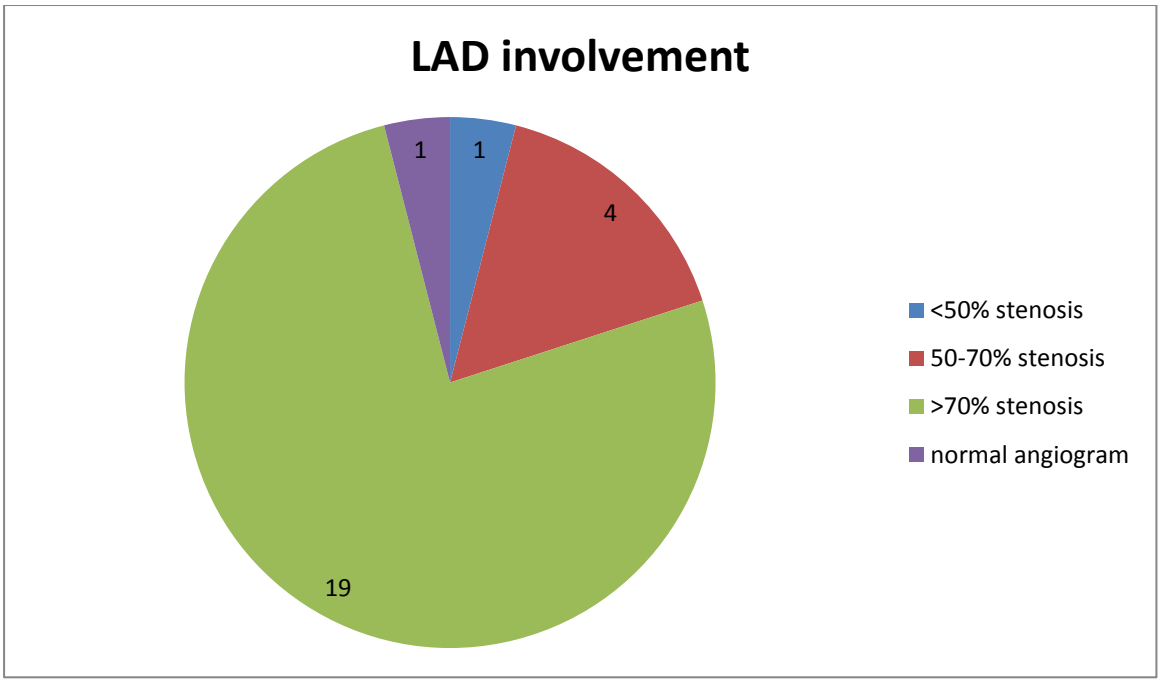

Fig.15 – Involvement of LAD

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C. INVOLVEMENT OF RIGHT CORONARY ARTERY: Out of the 25 RCAs which were assessed, 17 were diseased while 8 were normal. Of the diseased RCAs, 11 showed significant stenosis of more than 70%, 2 showed 50-70% stenosis and 4 showed minor disease with <50% stenosis. {Fig.16, Table.16 – Involvement of RCA}

Percentage of stenosis	*Frequency*	*Percent*
<50%	4	16
50-70%	2	8
>70%	11	44
Normal	8	32
Total	**25**	**100**

Table 16 – Involvement of RCA

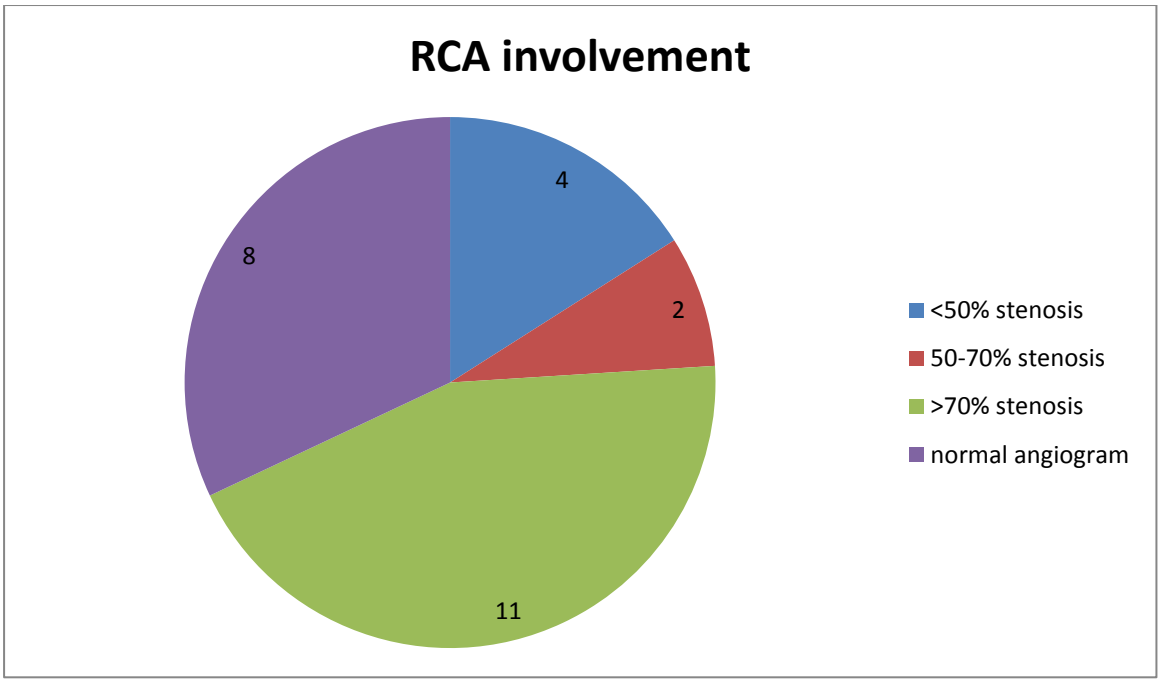

Fig.16 – Involvement of RCA

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D. <u>INVOLVEMENT OF LEFT CIRCUMFLEX ARTERY(LCX)</u>: Out of the 25 LCxs which were assessed, 14 were diseased while 11 were normal. Of the diseased LCxs, 7 showed significant stenosis of more than 70%, 2 showed 50-70% stenosis and 5 showed minor disease with <50% stenosis. {Fig.18, Table.18 – Involvement of LCx}

Percentage of stenosis	*Frequency*	*Percent*
<50%	5	20
50-70%	2	8
>70%	6	24
Normal	12	48
Total	**25**	**100**

Table 18 – Involvement of LCx

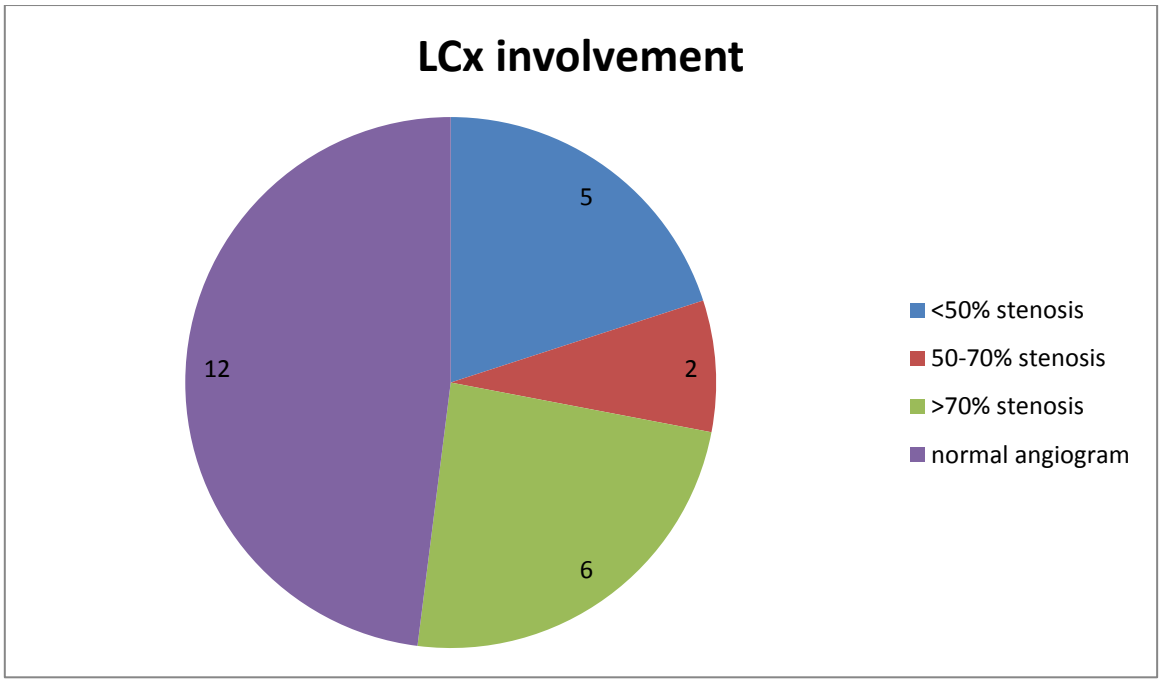

Fig.18 – Involvement of LCx

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DETECTION OF CAD USING MULTIPARAMETRIC CARDIAC MRI: Out of 84 patients who underwent stress cardiac MRI scan, 10 patients had both ischemia and infarction as evidenced by both stress perfusion defects and areas of delayed hyperenhancement. 6 patients had pure myocardial ischemia (presence of stress perfusion defect) without any evidence of infarction (i.e, no areas of delayed hyperenhancement). 34 patients had infarction alone without any evidence of ischemia. The rest of the 34 patients were MRI negative for CAD. In short, 50 patients were detected to have coronary artery disease by multiparametric cardiac MRI. {Fig.19, 20 ; Table.19, 20 – CAD assessment using multiparametric MRI}

Stress+Delayed	*Frequency*	*Percent*
Both yes	10	12
Stress Yes Delay No	6	7
Stress No Delay Yes	34	40.5
Both No	34	40.5
TOTAL	**84**	**100**

Table 19 – CAD positive on MRI

CAD positive on MRI	*Frequency*	*Percent*
Yes	50	60%
No	34	40%
TOTAL	84	100%

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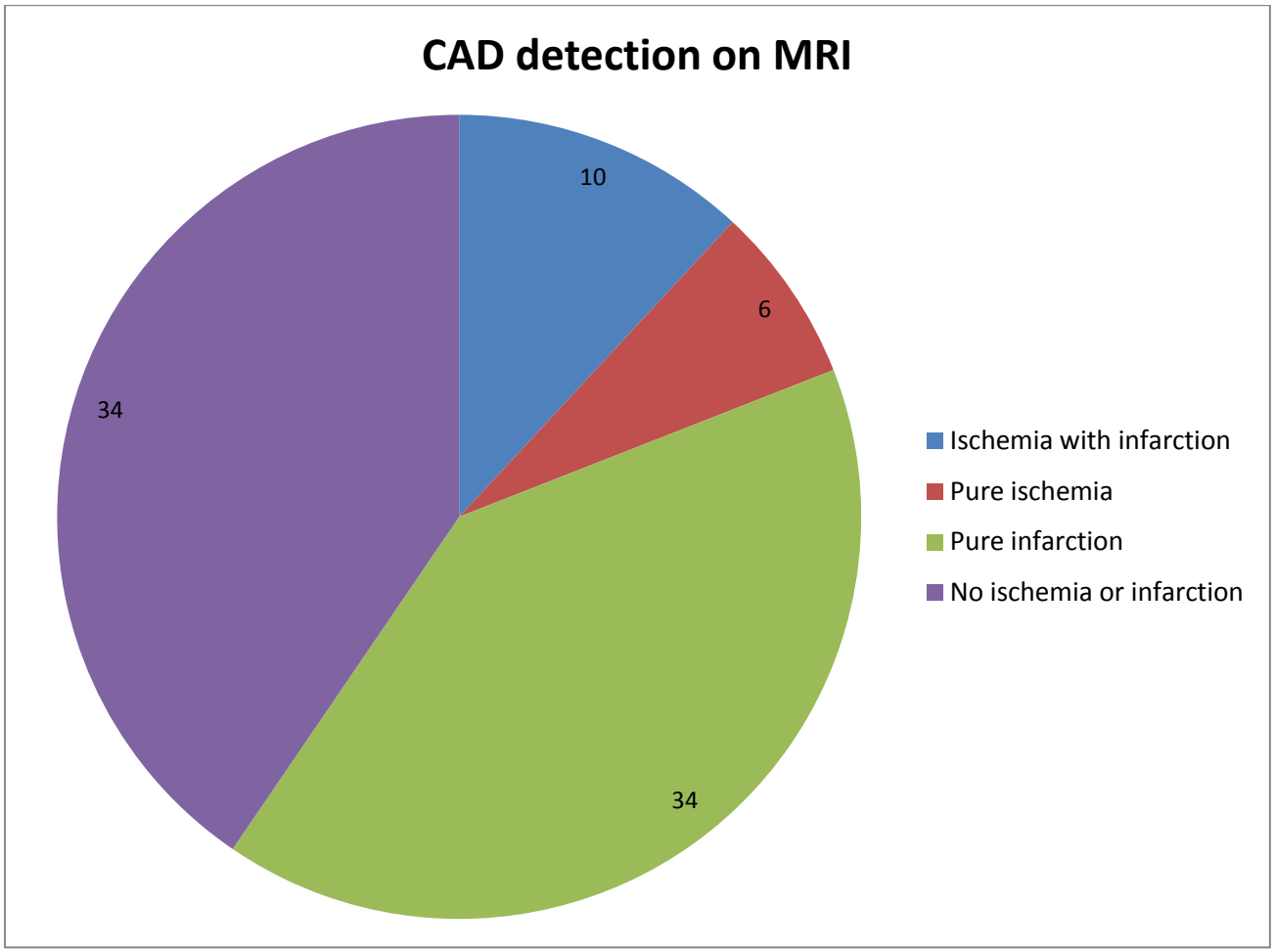

Fig.20 – Type of CAD on MRI

Type of CAD on MRI	*Frequency*	*Percent*
Ischemia with infarction	10	12
Ischemia only	6	7
Infarction only	34	40.5
No ischemia or infarction	34	40.5
TOTAL	84	100

Table 20 – Type of CAD on MRI

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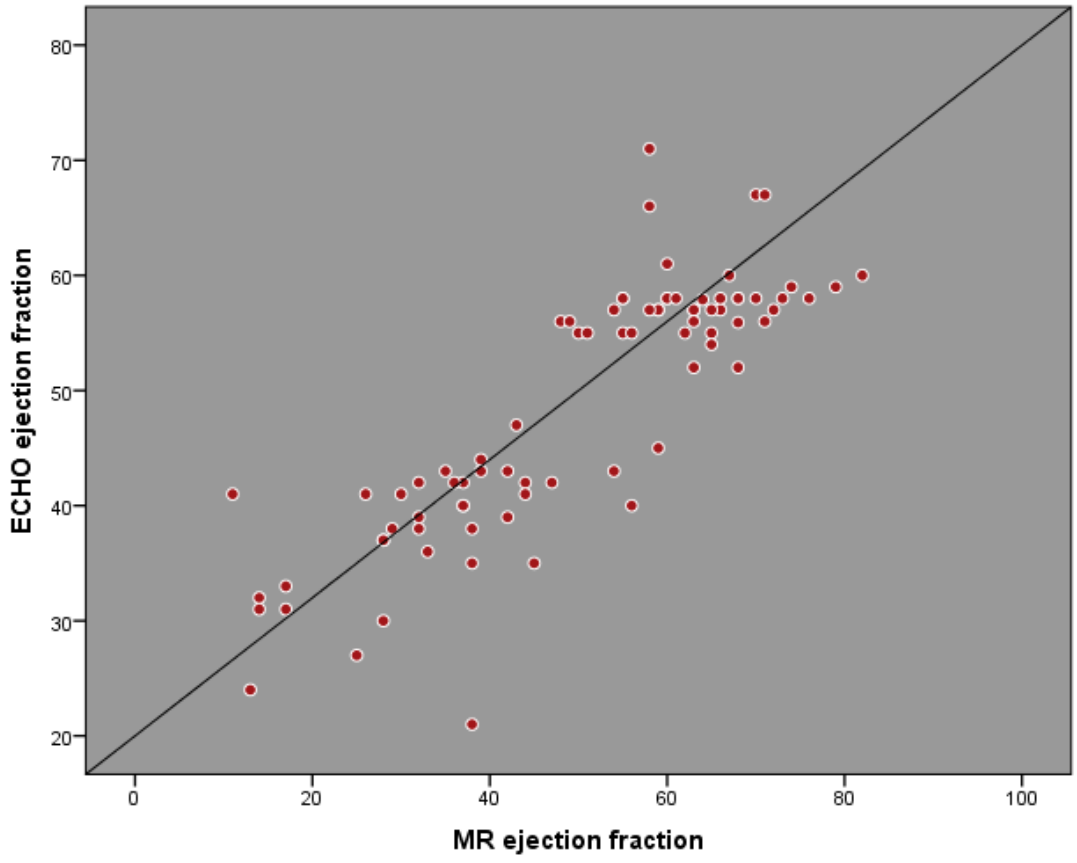
CORRELATION OF EJECTION FRACTION CALCULATED USING MRI AND ECHO: The ejection fraction calculated using MRI(MREF) and that calculated using ECHO(ECHOEF) was compared with each other. There was positive correlation between MREF and ECHOEF with a correlation coefficient of 0.851. {Table.21,Scatter plot – MR and ECHO ejection fraction}

	MR ejection fraction	ECHO ejection fraction
Mean	50.36	48.76
Standard deviation	17	11
Minimum	11	21
Maximum	82	71

Table.21 (above) & Scatter plot (below) of MR and ECHO ejection fraction



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ADVANTAGE OF USING STRESS AND DELAYED IN COMBINATION IN IDENTIFYING CORONARY ARTERY DISEASE: Out of total 25 patients who had coronary angiogram(CAG), 1 was normal. Out of the 24 positive angiograms, stress perfusion alone was able to identify only 10 (41.7%) whereas delayed enhancement identified 20 (83%). Using both stress perfusion and delayed enhancement as a diagnostic tool, the identification rate improved to 96%(23/24). {Fig.19, Table19 – MRI Vs CAG}

*Stress+Delayed * CAG*				
		CAG		Total
		positive	negative	
Stress+Delayed	Both yes	7	0	7
	StressYes DelayNo	3	0	3
	StressNo DelayYes	13	0	13
	Both No	1	1	2
Total		**24**	**1**	**25**

Table 19 – Stress & delayed with CAG

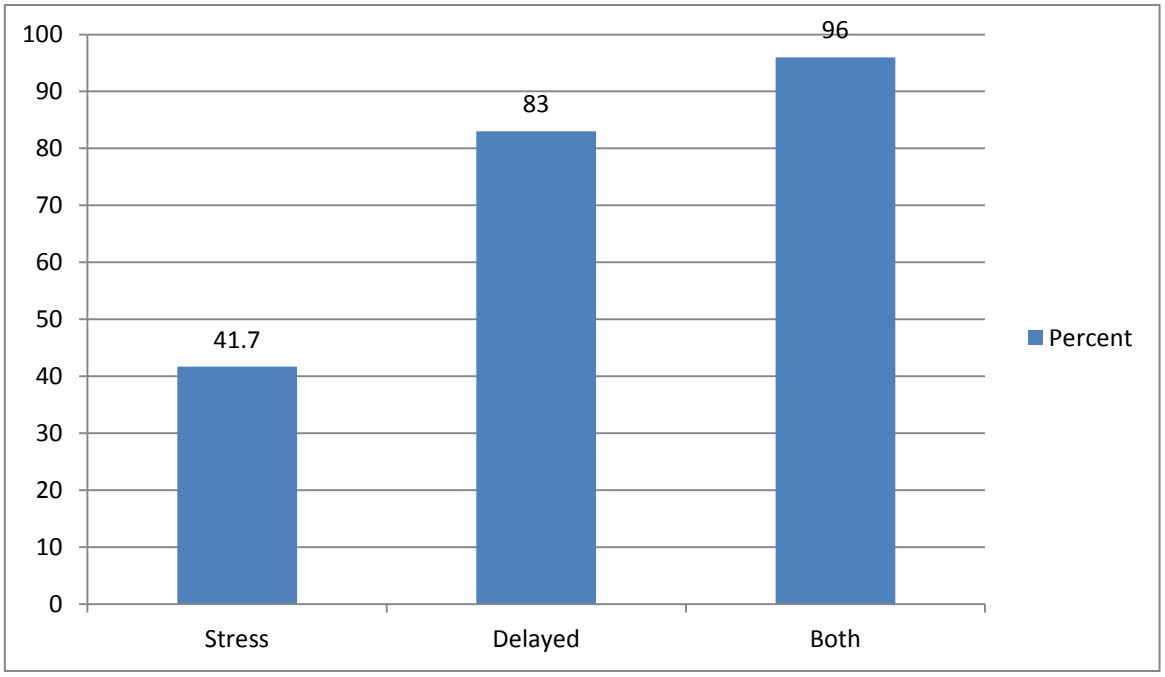

Fig. 19-Stress &delayed positive with CAG

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TERRITORIAL ANALYSIS OF FINDINGS IN MRI AND ANGIOGRAM

A. LAD TERRITORY: Out of the 23 diseased LADs identified on angiogram, 22 were detected using cardiac MRI using a combination of both stress and delayed scans.
B. RCA TERRITORY: Among the 13 diseased RCAs identified, 12 were identified using cardiac MRI study
C. LCx TERRITORY: This was found diseased in 10 patients. However, only 6 were accurately identified using cardiac MRI. Among the undetected 4 patients, 3 had co-existing RCA involvement. {Fig.20,Table.20 – Territorial analysis of MRI and CAG}

Stress + Delayed territory * Angiogram territory

		Angiogram Territory						Total
		LAD	RCA	LAD,RCA	LAD,LCx	LAD,RCA,LCx	normal	
Stress + Delayed Territory	LAD	6	0	1	1	0	0	8
	RCA	0	1	1	0	0	0	2
	LAD,RCA	0	0	2	1	2	0	5
	LAD,LCx	1	0	0	1	0	0	2
	LAD,RCA,LCx	0	0	1	0	5	0	6
	normal	1	0	0	0	0	1	2
Total		8	1	5	3	7	1	25

Table.20 – Territorial analysis of MRI and CAG

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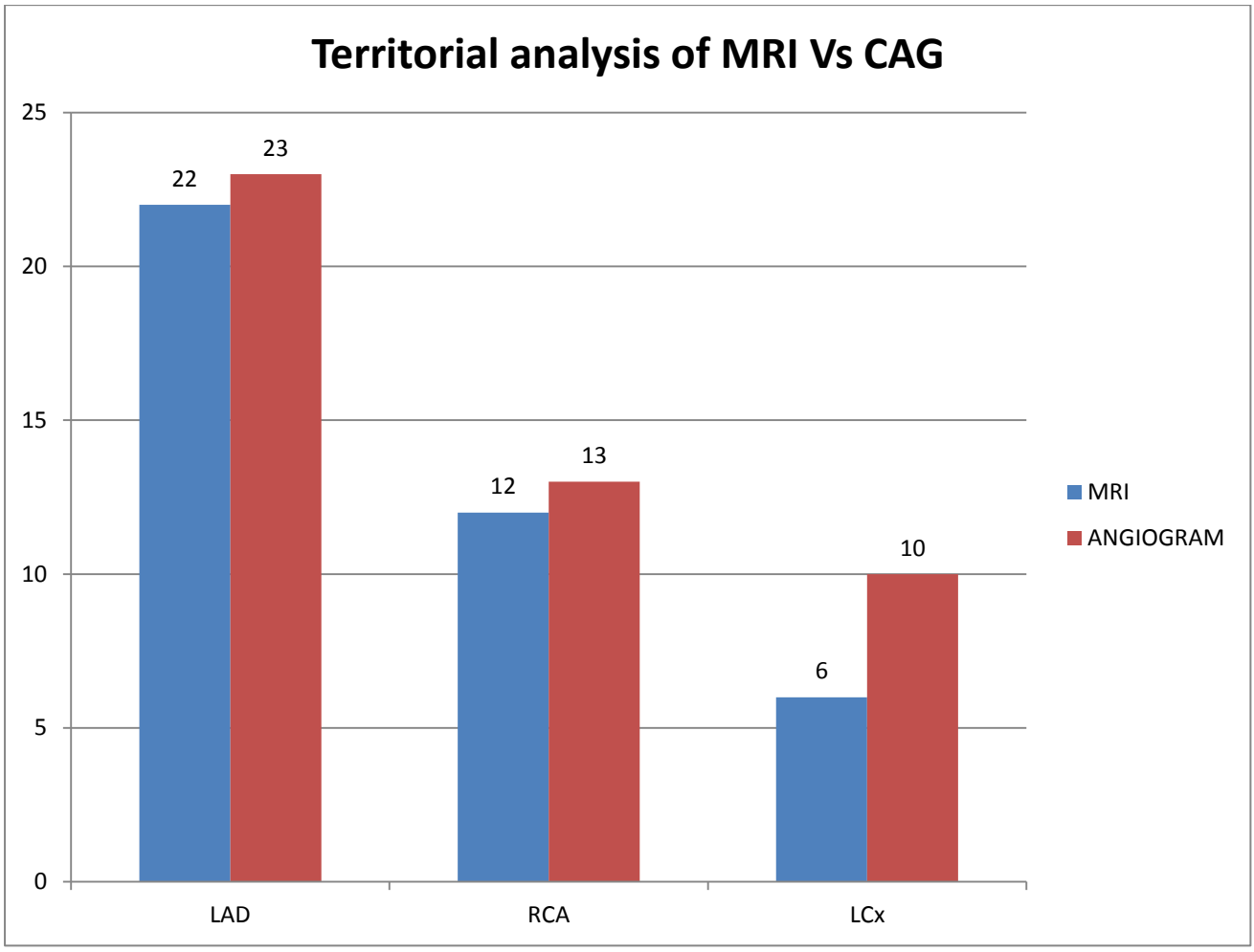
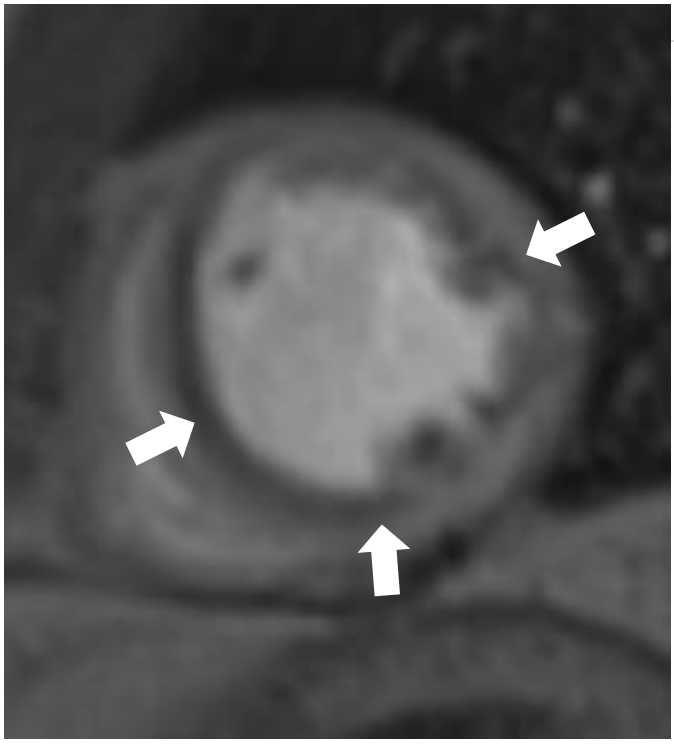
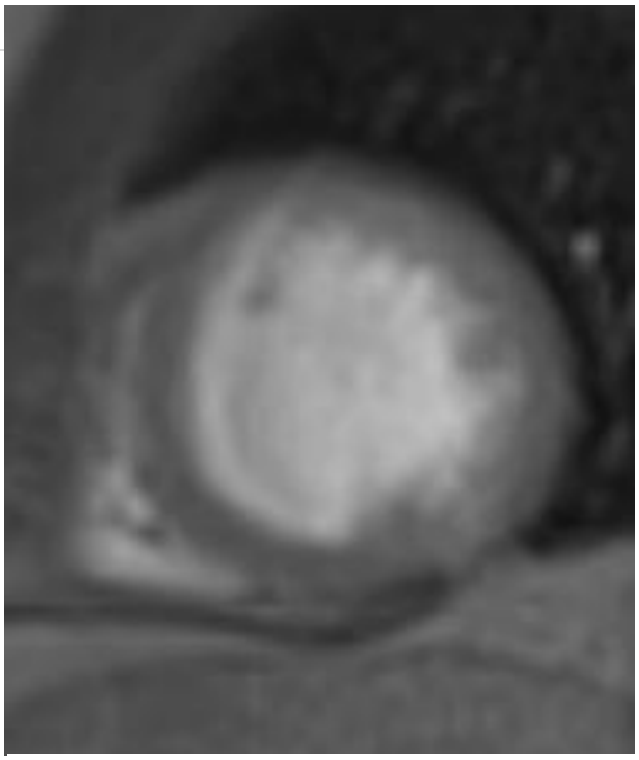


Fig. 20 – Territorial analysis of MRI and CAG

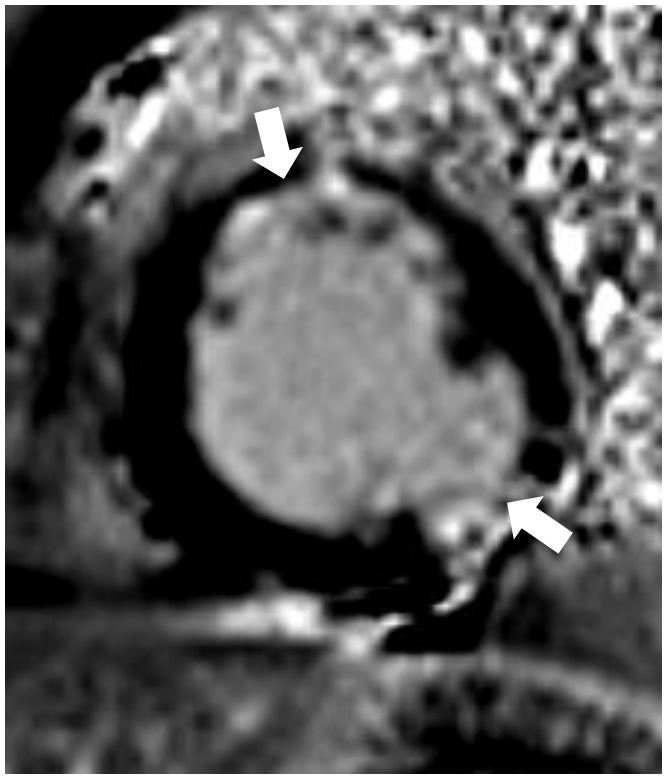


Stress scan with perfusion defect in the septal, inferior and lateral walls

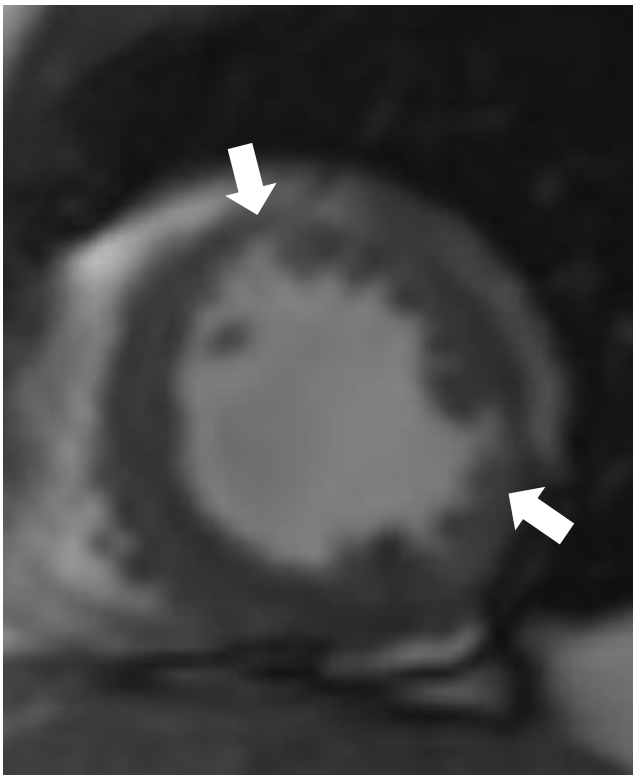


Rest scan with no perfusion defect

52 year old male with ischemia in all three territories and infarction in the anterior (LAD territory) wall and inferolateral (LCx territory) wall



Delayed enhancement in anterior and inferolateral walls and absence of delayed enhancement in the septal wall



Corresponding cine image showing thinning of myocardium in anterior and inferolateral walls

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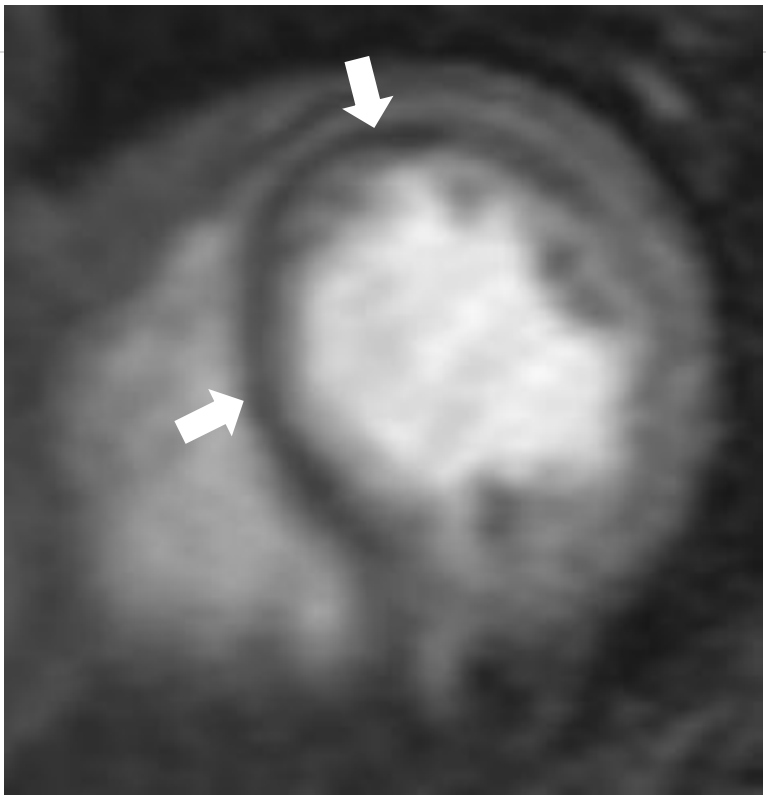
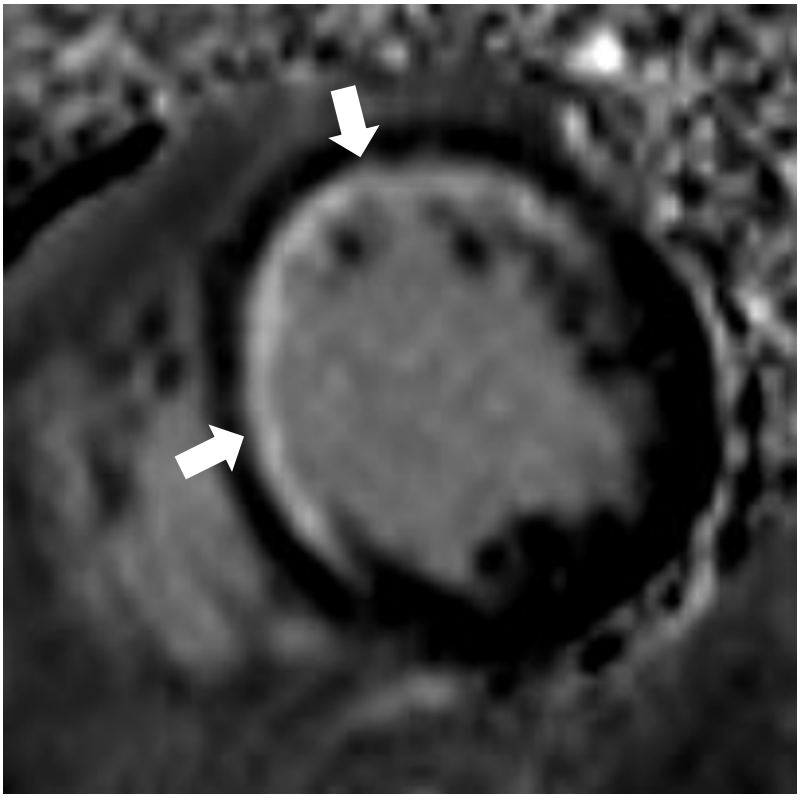


Stress scan with perfusion defect in the anterior and septal walls

58 year old male with a larger stress perfusion defect suggestive of an area of ischemia peripheral to the infarction in LAD territory



Delayed enhancement involving 26-50% of the anterior and septal walls

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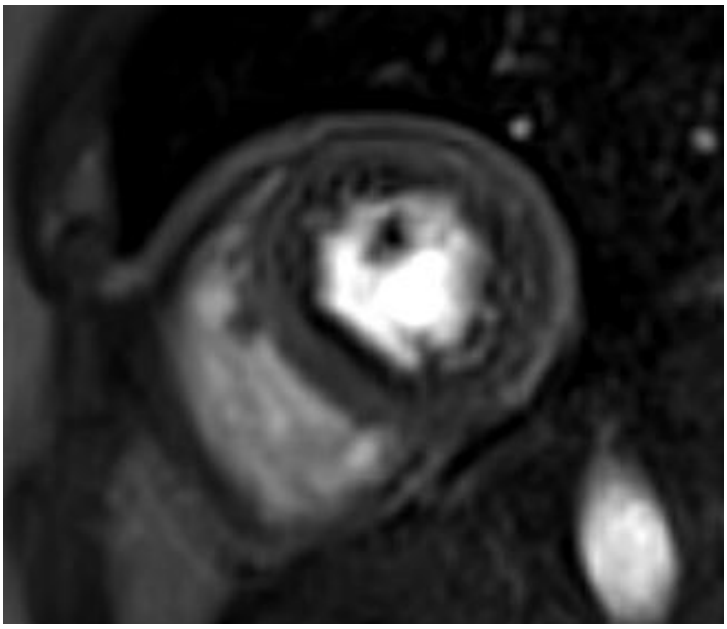
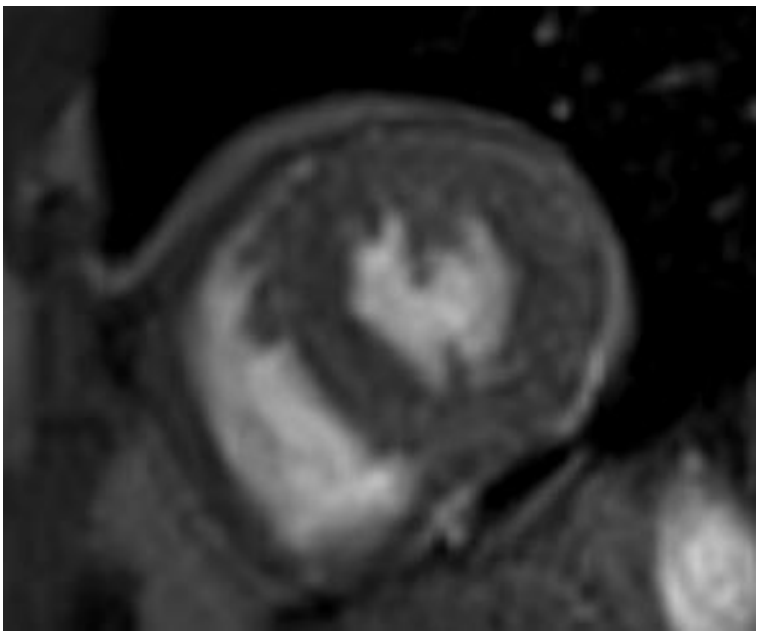
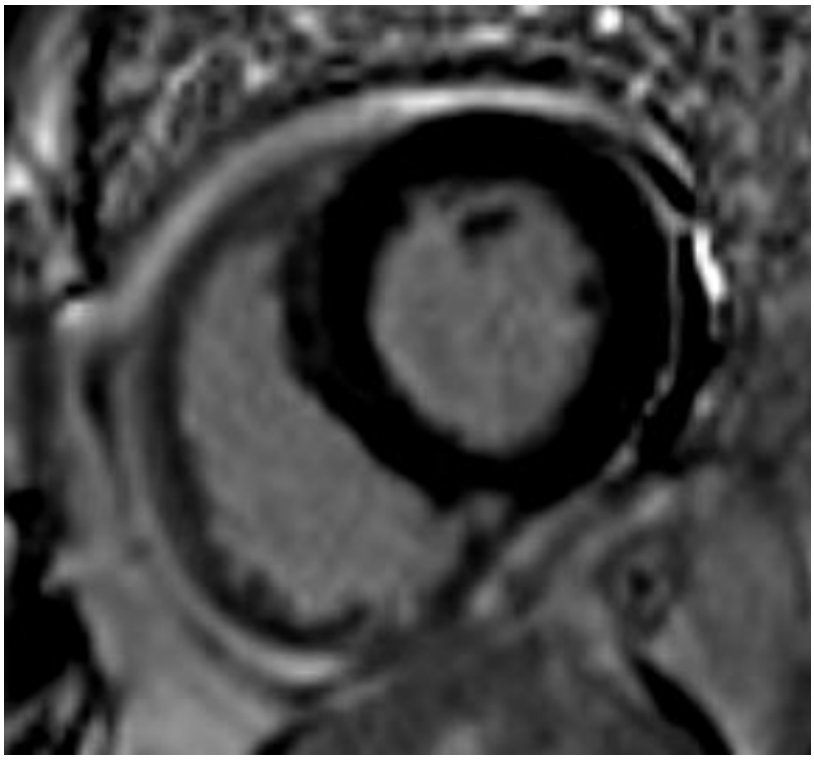


Stress scan with perfusion defect in the anteroseptal and inferoseptal walls



Rest scan with no perfusion defect in the anteroseptaland inferoseptal walls

57 year old male with ischemia in LAD and RCA territories



No evidence of delayed hyperenhancement suggestive of infarction

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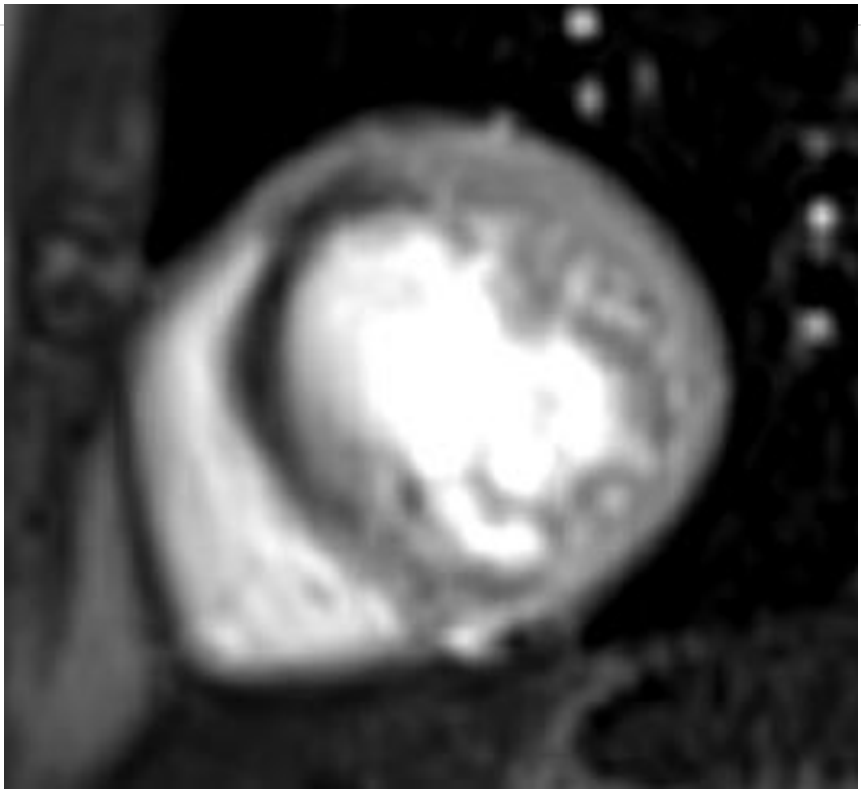
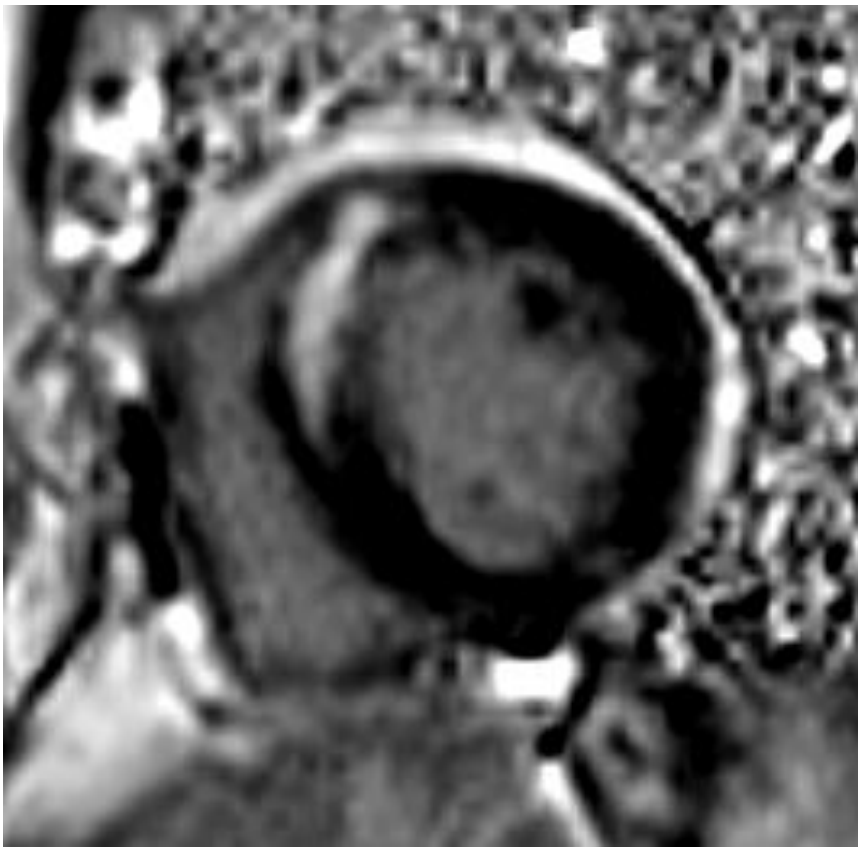


Stress scan with perfusion defect in the anterior and anteroseptal walls

62 year old male with a stress perfusion defect corresponding to the area of infarction suggestive of pure infarction in LAD territory



Delayed enhancement involving 76-100% of the anterior and anteroseptal walls

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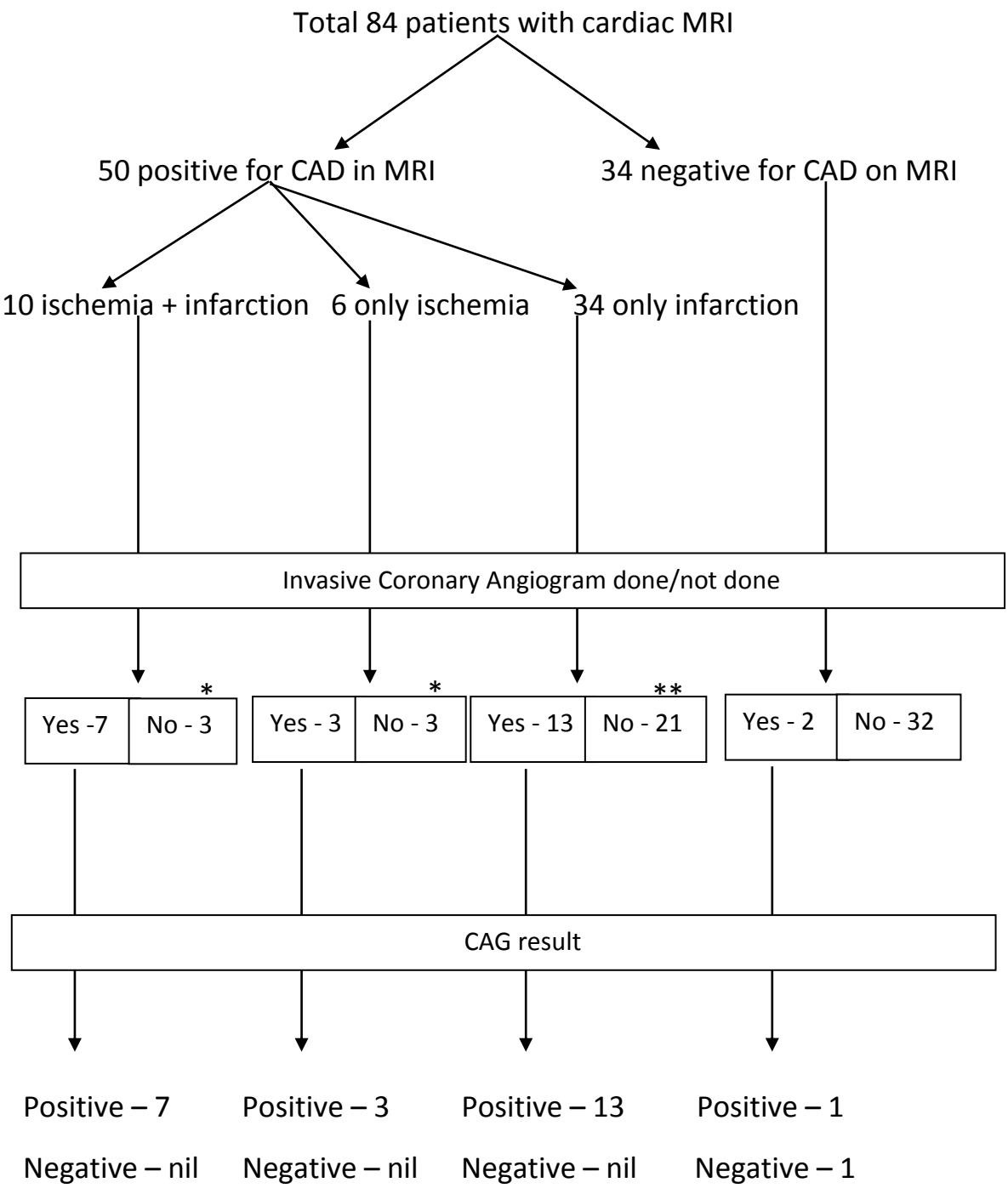
SUMMARY:



** 6 patients with ischemia on MRI study have no angiogram study as they were unwilling for an invasive angiogram.*

*** 21 patients with only infarction did not undergo invasive angiogram as they had non-viable myocardium on CMR*

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DISCUSSION:

A multiparametric cardiac MRI is an excellent tool to identify the presence of CAD. The main advantage is the completeness and the quality of information that it provides in a single step. The stress perfusion imaging can provide information regarding inducible myocardial ischemia while the delayed enhancement imaging assesses the myocardial viability. In addition, the cine images can assess wall motion abnormalities, ejection fraction and valves. Thus, it a one-stop shop for detection and assessment of CAD.

A high quality study can be completed within 40-50 minutes and this gives it an additional edge over most nuclear methods in terms of work efficiency. The study time is comparable to that of stress ECHO but with much more diagnostic information. The greatest advantage is its high image resolution (10 times better than SPECT) which makes it possible to distinguish endocardial and epicardial perfusion defects and in detecting left main disease, multivessel disease, and microvascular obstruction.

Our study included 84 patients with stress cardiac MRI and 25 patients with invasive angiograms. Out of the total 84 patients, 50 were MRI positive for CAD. Out of the 25 angiograms, one patient had normal study which was normal in cardiac MRI as well. In the rest of the 24 positive angiograms, one was not detected by cardiac MRI and rest all were CAD positive in both MRI and angiogram. Out of the 50 patients who were identified as ‘positive for CAD’ by cardiac MRI, 23 patients underwent coronary angiogram. All of these 23 patients had significant CAD according to invasive

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angiogram. This tells us that multiparametric cardiac MRI is an excellent tool for identification of significant CAD.

27 patients who were positive for CAD by MRI did not undergo an invasive coronary angiogram. These patients were either unwilling for an invasive CAG or had non-viable myocardium according to cardiac MRI.

The one patient (out of the 24 positive angiograms) whose CAD was undetected by cardiac MRI was a 75 year old male having diabetes and hypertension with significant stenosis (>70%) in the proximal LAD on CAG. The rest of the coronary vessels were normal. However, it was one of the earlier patients in our study to undergo cardiac MRI when our experience was less. On retrospective review of the MRI images, a stress perfusion defect was noted in the septal wall at basal level.

The territorial analysis revealed that diseased LADs and diseased RCAs had very high detection rate (22 out of 23 and 12 out of 13 for LAD and RCA respectively). LCx, on the other hand, was identified in only 6 out of 10 cases. However, 3 out of the 4 undetected diseased LCxs had co-existing RCA involvement. This is expected as there is significant overlap of LCx and RCA territories.

With use of adenosine, there were no major adverse events. 2 out of 84 had minor adverse effects. One had subjective chest discomfort which subsided without any active intervention. The other had symptoms of dyspnoes with rhonchi on examination which subsided after use of inhaled bronchodilator. This qualifies adenosine as a safe stress agent during our study.

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CONCLUSION:

It is evident that multiparametric cardiac MRI is a great tool for detection of CAD.

Adenosine stress perfusion scan can detect myocardial ischemia as evidenced by the presence of significant CAD in all those who underwent subsequent invasive angiogram.

Comparison of stress and rest perfusion scans can accurately differentiate between true perfusion defects and artefacts.

Late gadolinium enhancement showed excellent positive correlation with invasive angiogram in all 20 patients (this group includes those who had evidence of infarction on MRI and also underwent invasive angiogram)

Territorial analysis of MRI and invasive angiogram revealed that diseased LADs and RCAs were best detected by MRI. However, LCx had poorer correlation but this could be explained by the significant overlap between LCx and RCA territories.

Our study also adenosine as a safe stressor with only 2 (out of 84) patients developing minor complications, both of which subsided within minutes with nil or minimal intervention.

Adenosine stress cardiac MRI is a one stop shop for evaluation of patients with suspected or proven coronary artery disease - a single modality capable of defining cardiac anatomy and function, myocardial perfusion as well as myocardial viability.

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LIMITATIONS:

- Our study involved a relatively small sample size of 84 subjects
- Only 2 patients with normal cardiac MRI study underwent a subsequent invasive angiogram. This hinders the assessment of true negatives and false negatives in cardiac MRI test.

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ANNEXURE 1: CONSENT FORM AND INFORMATION SHEET IN ENGLISH

WRITTEN INFORMED CONSENT FORM

Date:

Study title: Assessment of coronary artery disease using Adenosine Stress cardiac MRI

It has been explained to me by the investigator in the language that I understand that this study is being carried out to diagnose whether the heart muscle is receiving enough blood flow, and whether or not there are areas of scarring from prior heart attacks. I have been told that it involves the use of a drug, adenosine which increases the amount of blood flow to the heart to look for signs of narrowing of the coronary arteries that supplies the heart muscle. The risks involved in the study have been explained to me. It has also been explained that I am free to withdraw from the study any time I want and this will not in any way compromise my treatment. I understand that my identity and participation will not be revealed in any information released to third parties.

Subjects' Name
Date of Birth/ Age:

i) I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions
ii) I understand my participation is purely voluntary and that I can withdraw from the study anytime, without any reason, without my medical care being affected.
iii) I understand that my identity will not be revealed in any information.
iv) I agree to take part in the above study.

Signature of subject Date

Name of the subject

Signature of the investigator Date

Name of the investigator

Signature of the witness Date

Name of the witness

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PATIENT INFORMATION SHEET

Study title: Assessment of coronary artery disease using Adenosine Stress cardiac MRI

The following information is provided to inform you about this study and your participation in it. Please read the information carefully and you are free to ask any questions regarding the study and the information given. The participation in this study is purely voluntary and you are free to withdraw from the study anytime.

Purpose of the study

Adenosine stress Cardiac MRI test is a non-invasive test which uses medication to increase the amount of blood flow to the heart to look for signs of narrowing of the coronary arteries that supply blood flow to the heart muscle. The images made by the MRI will allow your doctor to look at the anatomy and functioning of your heart.

Method to be followed

The test takes about 60 to 90 minutes. You will be asked to change into a hospital gown and remove all jewellery, dentures and hearing aids. Two intravenous (IV) lines will be placed into your arms. You will be connected to a blood pressure cuff and heart monitor. You will be moved onto a table that goes into the MRI scanner. The first 10 minutes, pictures will be taken to observe how your heart is working. Your heart will then be stressed with a medication called adenosine. This medication affects your heart in a manner similar to exercising, by increasing your heartbeat and blood pressure. An anaesthetist will be present in the scanner area while the medication is given. The medication will be stopped if you develop severe chest pain, severe shortness of breath or major changes in your heartbeat. After stopping the medication, any symptoms you are feeling will wear off very quickly. Rarely will you need medication to stop any chest pain, shortness of breath or slow heartbeat. While your heart is “stressed” you will be given a contrast agent called gadolinium-DTPA and a picture will be taken of your heart. This helps show areas of abnormal blood flow in your heart.

During the test, you will hear knocking sounds as the machine takes the pictures. We will also prompt you with instructions. For example, we may ask you to hold your breath for 8 to 10 seconds. It is important for you to stay as still as possible because movements can create glitches in the pictures.

Confidentiality

The participation in the study will remain confidential and shall be known only to the investigators.

Withdrawal from the study

Participation in this study is purely voluntary and you can withdraw from the study anytime without any reason. It will not compromise your treatment in any way. There won’t be any other risks involved in this study and you need not pay any extra money for the test.

For any queries, kindly contact- Dr. Subin Kuruvilla Thomas, PG Registrar, Department of Radiology, CMC Vellore.

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Detailed information about the Procedure

What is an adenosine magnetic resonance imaging stress test?

The magnetic resonance imaging (MRI) machine is a tube with a centre opening that is about three feet wide. A table slides into the central opening and the patient lies on the table. Pictures of the heart are created using a magnetic field, radio waves and computers. No X-rays are used to create the images. The images made by the MRI will allow your doctor to look at the anatomy and functioning of your heart. In addition, any areas of your heart not receiving a good supply of blood and any scarring of the heart muscle can be clearly seen. The test uses medication to increase the amount of blood flow to the heart to look for signs of narrowing of the coronary arteries that supply blood flow to the heart muscle.

What are the benefits and risks of the stress test?

This test will help your doctor diagnose whether your heart muscle is receiving enough blood flow, and whether or not there are areas of scarring from prior heart attacks. The risks of the test are very small and are associated with the medication that is used. When receiving adenosine, you may get facial flushing, mild headache, mild shortness of breath, chest tightness, arm or jaw discomfort, fast heartbeat/palpitations or slow heartbeat, low blood pressure, dizziness and light-headedness. It is important to tell your nurse how you feel during the test and if you are experiencing any of these symptoms. Although rare, complications can occur during this test and may include changes in your blood pressure or heart rhythm. Severe complications such as the possibility of heart attack and/or death are extremely rare. The careful monitoring of your blood pressure and continuous heart monitoring serve to minimize the small risks of the test.

Before the test

• Do not have any caffeine or tobacco for at least 24 hours before the test. (No tea, coffee, decaffeinated coffee, soft drinks or chocolate.

• You cannot have anything to eat or drink for 4 hours before your test.

• Take your medications as instructed by your doctor.

The day of the test

• The test takes about 60 to 90 minutes. Please allow at least 2 to 3 hours from the time you arrive to the time you leave.

• Bring a list of your current medications.

• Please arrive at MRI Room 3, one hour prior to the scheduled test time.

• You will be asked to change into a hospital gown and remove all jewellery, dentures and hearing aids.

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• Before the test starts, you will be asked questions about your medical history and the medication(s) you are taking. This is to make sure it is safe for you to have an MRI scan. The procedure will also be explained to you.

• Two intravenous (IV) lines will be placed into your arms. You will be connected to a blood pressure cuff and heart monitor so your blood pressure and heartbeat can be watched during the study. If there is a problem with these recordings, the test will be stopped.

• You will be moved onto a table that goes into the MRI scanner.

During the test

• The first 10 to 20 minutes, pictures will be taken to observe how your heart is working.

• Your heart will be stressed with a medication called adenosine. This medication affects your heart in a manner similar to exercising, by increasing your heartbeat and blood pressure. A doctor will be present in the scanner area while the medication is given. The medication will be stopped if you develop severe chest pain, severe shortness of breath or major changes in your heartbeat. After stopping the medication, any symptoms you are feeling will wear off very quickly. Rarely will you need medication to stop any chest pain, shortness of breath or slow heartbeat.

• While your heart is “stressed” you will be given a contrast agent called gadolinium-DTPA and a picture will be taken of your heart. This helps show areas of abnormal blood flow in your heart.

• After a short break, more pictures will be taken to look for any scarring of the heart muscle.

• During the test, you will hear knocking sounds as the machine takes the pictures. We will also prompt you with instructions. For example, we may ask you to hold your breath for 8 to 10 seconds.

• It is important for you to stay as still as possible because movements can create glitches in the pictures.

• At the end of the procedure, your IVs will be removed.

After the test

• You may resume your normal activity unless your doctor tells you differently.

• Take your regular medications as directed unless your doctor tells you differently.

• By the following day, the test results will be sent to the doctor who ordered the test. You will need to contact your doctor to discuss the results of your test.

• Keep any scheduled follow-up appointments with your primary doctor

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ANNEXURE 2: CONSENT FORM AND INFORMATION SHEET IN TAMIL

ஆய்வில் பங்கேற்பதற்கான தகவலறிந்த ஒப்புதல் வடிவம்

தேதி:
ஆய்வின் பெயர்: அடினோசின் ஸ்ட்ரெஸ் எம் ஆர் ஐ மூலம் இருதய இரத்தக் குழாய் நோயை மதிப்பிடுதல்
இந்த ஆய்வை பற்றிய விவரங்கள் நான் அறிந்த மொழியில் இனக்கு விவரிக்கப்பட்டன. இருதயத்தின் இரத்த ஓட்டம் சரியாக உள்ளதா என்பதையும் இருதயத்தில் ஏதேனும் தழும்புகள் உள்ளனவா என்பதைக் கண்டறிய இந்த ஆய்வு மேற்கொள்ளப்படுகிறது என்பதை நான் அறிவேன். மருந்துகள் மூலம் இருதயத்திற்கு செல்லும் இரத்த ஓட்டத்தை அதிகரித்து, அதன் மூலமாக இருதய தசைகளுக்கு செல்லும் இரத்த குழாய்கள் குறுகல் அடைந்துள்ளனவா என்பதைக் கண்டறிவதே இந்த ஆய்வின் நோக்கம் என்பதை நான் அறிவேன். இந்த ஆய்விலிருந்து நான் எந்த நிலையிலும் விலகிக்கொள்ளலாம் என்பதை நான் அறிவேன். என்னுடைய தனிப்பட்ட விவரங்கள் எந்த விதத்திலும் வெளியிடப்பட மாறாது என்பதை நான் அறிவேன்.

ஆய்வில் பங்குபெறுபவரின் பெயர்: _____

பிறந்த தேதி / வயது: _____

1 _____ தேதி அன்று நான் மேற்கூறிய ஆய்விற்கான தகவல் தாளைப் படித்து அதை புரிந்துகொண்டேன் என்று உறுதி அளிக்கிறேன். அது தொடர்பான கேள்விகள் கேட்க எனக்கு முழு வாய்ப்பு இருந்தது.

2 இந்த ஆய்வில் கலந்து கொள்வது ஒரு கட்டாயம் இல்லை என்பதையும், எந்த நிலையிலும் நான் இந்த ஆய்விலிருந்து எந்த காரணமும் அளிக்காமல் விலகிக்கொள்ளலாம் என்பதையும் நான் அறிவேன்.

3 இந்த ஆய்வை நடத்தும் அதிகாரிகள், மற்றும் இது தொடர்பான பிற அதிகாரிகள் என்னுடைய மருத்துவ விவரங்களை எனது அனுமதி இல்லாமலே கையாள உரிமை உள்ளவர்கள் என்பதை நான் அறிவேன். ஒரு வேளை நான் இந்த ஆய்வில் இருந்து விலகிக்கொண்டாலும் இது பொருந்தும் என்பதையும் நான் அறிவேன். இதற்கு நான் ஒப்புதல் அளிக்கிறேன். அனால் எதன் மூலம் என்னுடைய அடையாளம் வெளியாட்களுக்குத் தெரிவிக்கப்படமாட்டாது என்பதை அறிவேன்.

4 இந்த ஆய்வினால் வெளிவரக்கூடிய தகவல்கள் மற்றும் விளைவுகளை அறிவுயல் காரணங்களுக்காகப் பண்யன்படுதுவதை நான் தடுக்க மாட்டேன்.

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5 மேற்கூறிய ஆய்வில் பங்குகொள்ள நான் ஒப்புதல் அளிக்கிறேன்

ஆய்வில் பங்குபெறுபவரின் கையொப்பம் (அல்லது கைநாட்டை):

தேதி: _____ / _____ / _____

பெயர்: _____

கையொப்பம்:

ஆய்வு ஆராய்ச்சியாளரின் கையொப்பம்: _____

தேதி: _____ / _____ / _____

ஆய்வு ஆராய்ச்சியாளரின் பெயர்: _____

சாட்சி கையொப்பம்: _____

தேதி: _____ / _____ / _____

சாட்சியின் பெயர் & முகவரி: _____

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ஆய்வில் பங்குபெருபவருக்கான தகவல் தாள்

ஆய்வின் பெயர்: அடினோசின் ஸ்ட்ரெஸ் எம் ஆர் ஐ மூலம் இருதய இரத்தக் குழாய் நோயை மதிப்பிடுதல்

பின்வரும் விவரங்கள் மூலம் நீங்கள் இந்த ஆய்வைப் பற்றி அறிந்துகொள்ளலாம். இந்த தகவல் தாளை நன்கு படித்து விட்டு அது தொடர்பான சந்தேகங்களை எங்களிடம் தெரிவிக்கவும். இந்த ஆய்வில் பங்குபெறுவது ஒரு கட்டாயம் அல்ல.

ஆய்வின் நோக்கம்:

அடிநோசின் ஸ்ட்ரெஸ் இருதய எம் ஆர் ஐ என்பது உடல் ஆக்கிரமிப்பு அற்ற ஒரு பரிசோதனை முறை ஆகும். மருந்துகள் மூலம் இருதயத்திற்கு செல்லும் இரத்த ஓட்டத்தை அதிகரித்து, அதன் மூலமாக இருதய தசைகளுக்கு செல்லும் இரத்த குழாய்கள் குறுகல் அடைந்துள்ளனவா என்பதைக் கண்டறிவதே இந்த ஆய்வின் நோக்கம் ஆகும். எம் ஆர் ஐ மூலம் எடுக்கப்படும் படங்களைக் கொண்டகு உங்கள் இருதயத்தின் அமைப்பு மற்றும் இயக்கத்தை மருத்துவர் காண்பார்.

ஆய்வின் செயல்முறை:

இந்த ஆய்வு 60 முதல் 90 நிமிடங்கள் வரை நடைபெறும். நீங்கள் மருத்துவமனையில் வழங்கப்படும் ஆடைகளை அணிந்துகொள்ள வேண்டும். நகைகள், செயற்கை பற்கள், காது கேளாதோர் பயன்படுத்தும் இயந்திரம் ஆகியவற்றை நீங்கள் கழற்றி விட வேண்டும். உங்கள் கைகளில் இரண்டு ஊசிகள் செலுத்தப்படும். உங்கள் இரத்த அழுத்தம் மற்றும் இருதய துடிப்பு இயந்திரங்கள் மூலமாக சோதிக்கப்படும். நீங்கள் ஒரு மேஜை மேல் படுக்கவைக்கப்படுவீர்கள். அந்த மேஜை எம் ஆர் ஐ ஸ்கேன் செய்யும் இயந்திரத்துக்குள் செலுத்தப்படும். முதல் 10 நிமிடங்கள் உங்கள் இருதயத்தின் ஓட்டத்தை கண்டறிவதற்கான படங்கள் எடுக்கப்படும். பின்பு அடினோசின் எனப்படும் ஒரு மருந்தின் மூலமாக உங்கள் இருதயத்தின் அழுத்தம் அதிகரிக்கப்படும். உடற்பயிற்சி செய்யும் பொழுது உங்கள் இருதயம் மற்றும் இரத்த அழுததில் ஏற்படும் மாற்றங்களை ஒத்த விளைவுகளை இந்த மருந்து ஏற்படுத்தும். இந்த மருந்து செலுத்தப்படும் பொழுது, மயக்கம் அளிக்கும் சிறப்பு மருத்துவர் ஒருவர் இந்த நடைமுறைகளை மேற்பார்வை செய்வார். உங்களுக்கு நெஞ்சு வலி, மூச்சுத் திணறல் முதலியன நேரிட்டால் இந்த மருந்து உடனடியாக நிறுத்தப்படும். மருந்தை நிறுத்திய பின் இந்த அறிகுறிகள் விரைவாக நீங்கிவிடும். அரிதான சில நேரங்களில் மட்டுமே இவற்றை குணப்படுத்த கூடுதல் மருந்துகள் தேவைப்படும். உங்கள் இருதய அழுத்தம் மருந்து மூலமாக் அதிகரிக்கப்படும் பொழுது, கெடொலீனியம் DTPA எனப்படும் வேறு ஒரு மருந்து உங்களுக்கு செலுத்தப்படும். இதன் பின் மீண்டும் உங்கள் இருதயத்தின் படம் எடுக்கப்படும். இருதயத்தில் அசாதாரண இரத்த ஓட்டம் உள்ள இடங்களை இதன் மூலம் காண முடியும்.

இந்த பரிசோதனையில் இயந்திரம் படங்கள் எடுக்கும் நேரங்களில் உங்களுக்கு எதையோ தட்டுவதைப் போன்ற சத்தம் கேட்கும். அந்த நேரத்தில் நீங்கள் என்ன செய்ய வேண்டும் என்பதை நாங்கள் உங்களுக்கு சொல்லிக்கொண்டே

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இருப்போம். உதாரணத்திற்கு, 8 முதல் 10 நொடிகள் வரை உங்கள் மூச்சைப் பிடிதுக்கொள்ளுமாறு நாங்கள் கூறலாம். நீங்கள் எந்த வித அசைவும் என்றி நிலையாக இருப்பது மிகவும் அவசியம் ஆகும். நீங்கள் அசைந்தால் படங்களை தெளிவாக எடுக்க இயலாது.

நம்பகத்தன்மை:
நீங்கள் இந்த ஆய்வில் பங்குபெறுவது ஆய்வு அதிகாரிகளைத் தவிர வேறு ஒருவருக்கும் தெரிவிக்கப்பட மாட்டாது.

ஆய்விலிருந்து விலகுதல்:
இந்த ஆய்வில் பங்குபெற உங்களுக்கு எந்த வித கட்டாயமோ வற்புறுத்தலோ கிடையாது. உங்கள் முழு விருப்பத்தின் பேரில் மட்டுமே நீங்கள் இந்த ஆய்வில் பங்குபெற அழைக்கப்படுகிறீர்கள். ஒருவேளை உங்களுக்கு இந்த ஆய்வில் பங்குபெற விருப்பம் இல்லாவிட்டால், நீங்கள் இந்த ஆய்வில் இருந்து விலகிக் கொள்ளலாம். நீங்கள் அவ்வாறு விலகிக்கொண்டால், அது உங்கள் கண் நோய்க்கு இந்த மருத்துவமனையில் அளிக்கப்படும் சிகிச்சையை எந்த விதத்திலும் பாதிக்காது. இந்த ஆய்வில் பங்குபெருவதால் உங்களுக்கு எந்தவித கூடுதல் செலவும் கிடையாது.

உங்களுக்கு ஏதாவது சந்தேகங்கள் இருந்தால் நீங்கள் Dr சுபின் குருவில்லா தாமஸ்

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ஆய்வின் செயல்முறை பற்றிய விவரங்கள்:
எம் ஆர் ஐ என்பது காந்த இயக்கத்தைக் கொண்டு உடல் பாகங்களை ஸ்கேன் செய்யும் பரிசோதனை ஆகம். இந்த இயந்திரம் ஒரு குழாயைப் போல இருக்கும். இதன் நடுவில் மூற்று அடி அகலமுள்ள ஒரு பிளவு இருக்கும். நோயாளி ஒரு மேஜை மேல் படுக்கவைத்து இந்த இயந்திரத்துக்குள் அனுப்பப்படுவார். மின் காந்த அலைகள், ரேடியோ அலைகள் மற்றும் கணிப்பொறியைக் கொண்டு இருதயத்தின் படங்கள் எடுக்கப்படும். இந்த படங்கள் மூலம் உங்கள் இருதயத்தின் அமைப்பு மற்றும் செயல்பாடை அறிந்துகொள்ள முடியும். இருதயத்தில் இரத்த ஓட்டம் சரியாக இல்லாத இடங்கள் மற்றும் தழும்பான இடங்களை இதன் மூலம் கண்டறிய முடியும். மருந்துகள் மூலம் இருதயத்திற்கு செல்லும் இரத்த ஓட்டத்தை அதிகரித்து, அதன் மூலமாக இருதய தசைகளுக்கு செல்லும் இரத்த குழாய்கள் குறுகல் அடைந்துள்ளனவா என்பதைக் கண்டறிவதே இந்த பரிசோதனையின் நோக்கம் ஆகும்.

இந்த பரிசோதனையின் பழங்கள் மற்றும் அபாயங்கள் என்னென்ன?
உங்கள் இருதயத்தின் இரத்த ஓட்டம் சரியாக உள்ளதா என்றும், உங்கள் இருதயத்தில் ஏதேனும் தழும்புகள் உள்ளனவா என்றும் இந்த பரிசோதனையின் மூலம் கண்டறிய முடியும். வெகு அரிய சில நேரங்களில் மட்டுமே இந்த மருந்துகளின் மூலமாக பக்க விளைவுகள் ஏற்படும். அடினோசின் மருந்து செலுத்தப்படும் பொது முகம் சிவத்தல், லேசான தலைவலி, லேசான மூச்சு கஷ்டம், நெஞ்சு அழுத்தம், கை மற்றும் தாடை அசௌகரியம், இதயத்துடிப்பு அதிகரித்தல், இரத்த அழுத்தம் குறைதல் மற்றும் தலை சுற்றல் ஏற்பட வாய்ப்புள்ளது. உங்களுக்கு இதுபோன்ற ஏதேனும் அறிகுறிகள் இருந்தால், உங்கள் அருகில் உள்ள செவிலியரிடம் அவற்றைத் தெரிவிக்க வேண்டும். வெகு அரிய சில நேரங்களில் இருதய இயக்கம் மற்றும் இரத்த அழுததில் சிக்கல்கள் ஏற்படலாம். மாரடைப்பு மற்றும் மரணம் போன்ற அபாயங்கள் நிகழ்வது மிகவும் அரிதாகும். உங்கள் இருதய துடிப்பு மற்றும் இருதய அழுததை தொடர்ந்து கண்காணிப்பதால் இந்த அபாயங்கள் நிகழ்வதை வெகுவாக குறைத்து விடலாம்.

பரிசோதனைக்கு முன்னால்:

- *பரிசொதனைக்குக் குறைந்தது 24 மணி நேரங்களுக்கு முன்பிலிருந்து புகை பிடித்தல், தேநீர், காபி, குளிர் பானங்கள், சாக்லேட் முதலியவற்றை தவிர்க்க வேண்டும்*
- *பரிசொதனைக்குக் 4 மணி நேரங்களுக்கு முன்பிலிருந்து எதையும் சாப்பிடவோ குடிக்கவோ கூடாது.*
- *உங்கள் மருத்துவரின் ஆலோசனையின் படி உங்கள் மருந்துகளை சாப்பிடவும்*

பரிசோதனை தினத்தன்று:

- *பரிசோதனை முடிய 60 முதல் 90 நிமிடங்கள் எடுக்கும். நீங்கள் மருத்துவமனையில் குறைந்தது 2 முதல் 3 மணி நேரங்கள் தங்கி இருக்கத் தேவைப்படும்*
- *நீங்கள் சாப்பிடும் எல்லா மருந்துகளையும் பட்டியல் இட்டு எடுத்து வரவும்*

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- உங்களுக்கு குறிக்கப்பட்ட நேரத்திற்கு ஒரு மணி நேரம் முன்பே எம் ஆர் ஐ அரை எண் 3 கு வரவும்
- நீங்கள் மருத்துவமனையில் வழங்கப்படும் ஆடைகளை அணிந்துகொள்ள வேண்டும். நகைகள், செயற்கை பற்கள், காது கேளாதோர் பயன்படுத்தும் இயந்திரம் ஆகியவற்றை நீங்கள் கழற்றி விட வேண்டும்.
- பரிசோதனைக்கு முன்னால் உங்கள் உடல் நிலை மற்றும் நீங்கள் சாப்பிடும் மருந்துகளைப் பற்றி சில கேள்விகள் கேட்கப்படும். இந்த பரிசோதனை உங்களுக்கு பாதுகாப்பானது என்பதை உறுதி செய்துகொள்ளவே இவை கேட்கப்படும். பரிசோதனை செயல்முறைகளும் உங்களுக்கு விளக்கப்படும்.
- உங்கள் கைகளில் இரண்டு ஊசிகள் செலுத்தப்படும். உங்கள் இரத்த அழுத்தம் மற்றும் இருதய துடிப்பு இயந்திரங்கள் மூலமாக சோதிக்கப்படும். அவற்றில் ஏதேனும் பிரச்சினை ஏற்பட்டால் பரிசோதனை நிறுத்தப்படும்.
- நீங்கள் ஒரு மேஜை மேல் படுக்கவைக்கப்படுவீர்கள். அந்த மேஜை எம் ஆர் ஐ ஸ்கேன் செய்யும் இயந்திரத்துக்குள் செலுத்தப்படும்.
- முதல் 10 முதல் 20 நிமிடங்கள் உங்கள் இருதயத்தின் ஓட்டத்தை கண்டறிவதற்கான படங்கள் எடுக்கப்படும்.
- பின்பு அடினோசின் எனப்படும் ஒரு மருந்தின் மூலமாக உங்கள் இருதயத்தின் அழுத்தம் அதிகரிக்கப்படும். உடற்பயிற்சி செய்யும் பொழுது உங்கள் இருதயம் மற்றும் இரத்த அழுததில் ஏற்படும் மாற்றங்களை ஒத்த விளைவுகளை இந்த மருந்து ஏற்படுத்தும். இந்த மருந்து செலுத்தப்படும் பொழுது, மயக்கம் அளிக்கும் சிறப்பு மருத்துவர் ஒருவர் இந்த நடைமுறைகளை மேற்பார்வை செய்வார். உங்களுக்கு நெஞ்சு வலி, மூச்சுத் திணறல் முதலியன நேரிட்டால் இந்த மருந்து உடனடியாக நிறுத்தப்படும். மருந்தை நிறுத்திய பின் இந்த அறிகுறிகள் விரைவாக நீங்கிவிடும். அரிதான சில நேரங்களில் மட்டுமே இவற்றை குணப்படுத்த கூடுதல் மருந்துகள் தேவைப்படும்.
- உங்கள் இருதய அழுத்தம் மருந்து மூலமாக் அதிகரிக்கப்படும் பொழுது, கெடொலீனியம் DTPA எனப்படும் வேறு ஒரு மருந்து உங்களுக்கு செலுத்தப்படும். இருதயத்தில் அசாதாரண இரத்த ஓட்டம் உள்ள இடங்களை இதன் மூலம் காண முடியும். இதன் பின் இருதயத்தில் ஏதேனும் தழும்புகள் உள்ளனவா என்று கண்டறிய மீண்டும் படங்கள் எடுக்கப்படும்.
- இயந்திரம் படங்கள் எடுக்கும் நேரங்களில் உங்களுக்கு எதையோ தட்டுவதைப் போன்ற சத்தம் கேட்கும். அந்த நேரத்தில் நீங்கள் என்ன செய்ய வேண்டும் என்பதை நாங்கள் உங்களுக்கு சொல்லிக்கொண்டே இருப்போம். உதாரணத்திற்கு, 8 முதல் 10 நொடிகள் வரை உங்கள் மூச்சைப் பிடிதுக்கொள்ளுமாறு நாங்கள் கூறலாம்.
- நீங்கள் எந்த வித அசைவும் என்றி நிலையாக இருப்பது மிகவும் அவசியம் ஆகும். நீங்கள் அசைந்தால் படங்களை தெளிவாக எடுக்க இயலாது.

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- *பரிசோதனை முடிந்த பின்பு உங்கள் கைகளில் செலுத்தப்பட்ட ஊசிகள் அகற்றப்படும்.*

பரிசோதனைக்குப்பின்:

- *உங்கள் மருத்துவர் வேண்டாம் என்று சொன்னாலே ஒழிய உங்கள் வழக்கமான வேலைகளை நீங்கள் தொடரலாம்*
- *உங்கள் மருத்துவர் வேண்டாம் என்று சொன்னாலே ஒழிய நீங்கள் உங்கள் வழக்கமான மருந்துகளை சாப்பிடலாம்*
- *உங்கள் பரிசோதனைகளின் முடிவுகள் உங்கள் மருதுரவுக்கு மறு நாளே அனுப்பி வைக்கப்படும். இவற்றைப் பற்றிய தகவல்களை உங்கள் மருத்துவரிடம் நீங்கள் கேட்டு அறிந்து கொள்ளலாம்.*
- *உங்களை இந்த பரிசோதனைக்காக அனுப்பிய மருத்துவரை மீண்டும் சந்திக்க முன்பதிவு செய்து வைத்துக் கொள்ளுங்கள்.*

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ANNEXURE 3: RAW DATA

sno	Age	Sex	Diabetic	Hyperten	Dyslipide	Indication	oldMI	oldstent	oldCABG	stressonly	Stressonly	Circumfer	stressrest	stressrest	delayed	delayedTe	stress_del	DelayedLA	DelayedRI	DelayedLC	Delayedpa
1	30	1	2	1	1	1	2	2	2	2	8	1	2	8	2	8		5	5	5	2
2	61	2	2	1	1	1	2	2	2	2	8	1	2	8	2	8		5	5	5	2
3	44	2	1	1	1	2	1	2	2	2	8	1	1	2	1	5	5	4	5	4	2
4	41	2	1	1	2	2	1	2	2	2	8	2	2	8	1	2		5	4	5	2
5	41	2	2	2	2	1	2	2	2	2	8	2	1	1	2	8		5	5	5	2
6	62	1	2	1	2	1	2	2	2	2	8	1	2	8	2	8		5	5	5	2
7	63	2	2	1	2	1	2	2	2	2	8	2	2	8	2	8		5	5	5	2
8	43	1	2	2	2	2	1	2	2	2	8	2	2	8	1	1		4	5	5	2
9	67	1	1	2	1	1	2	2	2	2	8	2	2	8	2	8		5	5	5	2
10	49	1	2	1	2	1	2	2	2	2	8	2	2	8	2	8		5	5	5	2
11	52	2	1	2	2	1	2	2	2	2	8	2	2	8	2	8		5	5	5	2
12	75	1	1	1	2	1	2	2	2	2	8	2	2	8	2	8	8	5	5	5	2
13	65	2	1	2	1	1	2	2	2	2	8	2	2	8	2	8		5	5	5	2
14	60	2	1	1	1	1	2	2	2	2	8	1	2	8	2	8		5	5	5	2
15	57	1	2	2	2	2	1	2	2	2	8	2	2	8	1	1		4	1	5	2
16	43	1	1	1	1	1	2	2	2	2	8	2	2	8	1	1	1	3	5	5	2
17	65	2	2	1	1	1	2	2	2	2	8	2	2	8	1	4	4	4	3	5	2
18	61	1	1	2	2	2	1	2	1	1	4	2	2	8	2	8	4	5	5	5	2
19	62	1	2	2	2	1	2	2	2	2	8	2	1	7	2	8		5	5	5	2
20	61	1	2	1	2	2	1	2	2	1	2	2	2	8	1	2	2	5	2	5	2
21	54	1	2	2	2	2	1	2	2	1	3	2	2	8	1	4		4	4	5	2
22	75	1	2	2	2	1	2	2	2	2	8	2	2	8	1	4		4	4	5	2
23	56	1	2	1	2	1	2	2	2	2	8	2	1	1	2	8	8	5	5	5	2
24	49	1	2	2	2	1	2	2	2	2	8	2	1	1	2	8		5	5	5	2
25	51	2	2	1	1	1	2	2	2	2	8	2	2	8	2	8		5	5	5	2
26	72	1	2	1	2	2	2	2	2	2	8	2	2	8	2	8		5	5	5	2
27	50	1	1	2	2	2	1	2	1	2	8	2	2	8	1	1		4	5	5	2
28	69	2	2	1	2	1	2	2	2	1	1	2	2	8	2	8		5	5	5	2
29	47	1	1	2	1	1	2	2	2	2	8	2	2	8	2	8		5	5	5	2

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Wallmotic	Wallmotic	Hypertroc	MRLVEF	ECHOLVEF	AngioPost	AngioLAD	ProxLAD	DistalLAD	TypeofLAI	AngioRCA	ProxRCA	DistalRCA	AngioLCx	ProxLcx	DistalLCx	atypicalco	atypicalle	AngioTerr	typeofCAI	Complicat	MajorCom	MinorCon	Treatmen	GS	stress_del
2	8	1	79	59	3															2	3	4	4		4
2	8	2	68	58	3															2	3	4	4		4
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1	2	2	55	58	3															2	3	4	4		3
2	8	2	63	57	3															2	3	4	4		4
2	8	1	48	56	3															2	3	4	4		4
2	8	2	55		3															2	3	4	4		4
1	1	2	63	52	3															2	3	4	4		3
2	8	2	63	57	3															2	3	4	4		4
2	8	1	70	67	3															2	3	4	4		4
2	8	1	59	57	3															2	3	4	4		4
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2	8	2	65	55	3															2	3	4	4		2
2	8	1	72	57	3															2	3	4	4		4

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1	4	2	35	43	3																	2	3	4	4		3
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2	8	2	65	54	3																2	3	4	4		4
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